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A CASE OF DISLOCATION OF THE ATLAS,

SHOWN BY A SKIAGRAM, CAUSING PARALYSIS OF THE LEFT ARM AND THE SYRINGOMYELIC DISSOCIATION SYMPTOM ON THE OPPOSITE SIDE.

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of Philadelphia.

Some years ago I put on record two cases of trauma of the cervical region of the spinal cord simulating syringomyelia.[1] These cases were illustrated with photographs, and eventually post-mortem findings were reported in both of them. By a coincidence each of these patients had sustained two severe accidents quite dissimilar in type, and these accidents had resulted in fracture and dislocation of some of the cervical vertebræ, with marked deformity of the neck. Both cases had been of a goodly number of years' duration.

The fact of special interest in those two cases was the close similarity which they presented to the now well-known and classical picture of syringomyelia. Syringomyelia was not quite so well known ten years ago as it is now; and in fact, although here in Philadelphia we had been fairly prompt in recognizing and recording some cases of it, the disease was still rare enough to be interesting. A case of my own in 1893 was one of the first published in America with full microscopic findings. My recollection is that the disease was not much talked of nor widely recognized in this country before

[1] Traumatic Affections of the Cervical Region of the Spinal Cord Simulating Syringomyelia, Journal of Nervous and Mental Disease, June, 1894, p. 345. A Study of the Lesions in a Case of Trauma of the Cervical Region of the Spinal Cord Simulating Syringomyelia, Brain, 1898, xxi. p. 21. A Study of the Lesions in a Second Case of Trauma of the Cervical Region of the Spinal Cord Simulating Syringomyelia, Journal of Nervous and Mental Disease, February, 1900, p. 65.

1892 and 1893, although it was known in a general way from the reports of a few European observers, especially Leyden, but regarded rather as a pathological curiosity. Gowers' first edition, published in 1886, contains a fairly good anatomical description, but a very inadequate clinical account. In Bruhl's monograph on syringomyelia, printed in 1890, there is a noteworthy scarcity of American names in the extensive bibliography, not because of French indifference to American work, but because very little American work in this field had been done. Van Gieson, of New York, had published some autopsical findings in 1889, and he was probably the first American in the field with a microscope. Mere clinical reports of a few cases that may have been syringomyelia had been made by a few American observers, but they had not been confirmed, by autopsy.

I mention these few facts merely to show how little had been seen at that time of what I may call the syringomyelic syndrome; certainly it was a rare thing, if not unprecedented, to find this syndrome in two cases, both of them due to trauma, and neither of them presenting a cavity formation in the cord.

But a further and special point of interest in those two cases was in the fact that they both presented lesions which were partially unilateral, that is, of a unilateral type, and this fact led to some interesting conclusions on the subject of sensory conduction in the spinal cord.

The observations, briefly stated, were as follows: The dissociation symptom, or rather the thermoanæsthesia and analgesia, were present on the side *opposite* the main lesion, while tactile anæsthesia, with involvement of the motor tracts, was present *on the side* of the lesion. This was so in both those cases. I discussed at length, in my reports of those two cases, the grounds for supposing that these symptoms indicated that the fibres for the heat and cold senses and for pain, passing in by the posterior roots, decussate in the gray matter and pass upward in the anterolateral tracts of the opposite side, while the fibres for simple touch pass up in the posterior columns without decussating. This seems to be the obvious explanation of the symptoms. It suggests also that our conception of the Brown-Séquard syndrome will have to be modified to the extent of recognizing that tactile anæsthesia and thermoanæsthesia and analgesia are not of necessity present on the one side, but on opposite sides. These reasons in detail it is hardly necessary to repeat here; they can be read in the original papers.

The case which I have to put on record in this paper presents some points of marked resemblance to the other two, and also one or two features that seem to be quite unique. The man has been under my care in the Methodist Hospital for several months, and, as in the other cases, he has suffered from not only one but two

very severe and successive injuries. I am indebted to Dr. Imboden, the resident physician, for clinical notes.

J. W., aged twenty-one years, admitted January 12, 1904. Born in Philadelphia and has resided here during entire life. Uses tobacco in moderation, but alcohol to excess.

Previous Medical History. So far as he knows he never had any of the usual diseases of childhood except pertussis.

Previous Surgical History. When thirteen years of age he bruised the left leg below the knee while riding a bicycle, and this accident required the removal of some necrotic bone in this region. On the 16th of September, 1903, he had been drinking quite heavily in the morning, and while driving on a cart he fell off during an attempt to check the horse, which had become somewhat unmanageable. He struck on his left shoulder, the cart-wheel passing over the back of his neck. He was unconscious for an indeterminate period, being brought into the surgical dispensary of the Methodist Hospital, and a fracture of the jaw was diagnosed, but no spinal injury was recognized. He was sent to the surgical ward and remained there twelve days, and after his discharge he continued to come to the dispensary and was treated for an abscess of the jaw, presumably a result of infection through the mouth incident to or as a result of the fracture of the jaw. During all this time he was unable to turn the head without at the same time rotating the shoulders, and there can be little doubt that his spine had been injured in this first accident.

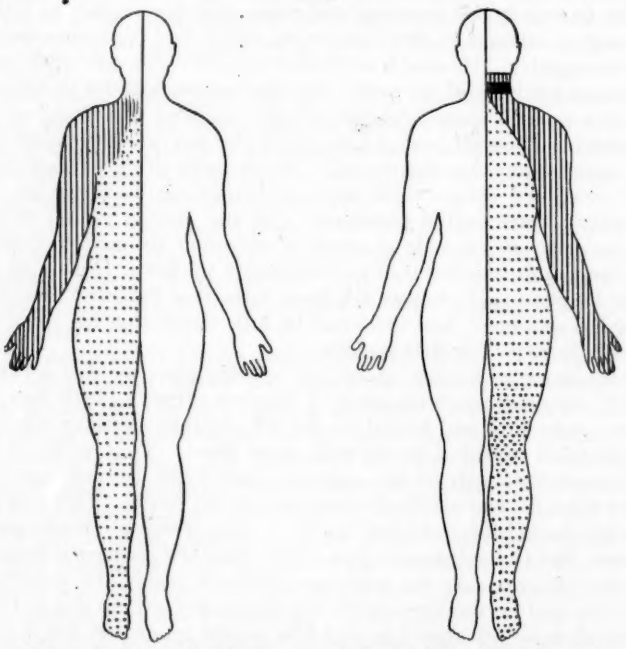
On January 12, 1904, about four months after the first accident, while the man was walking on a slippery sidewalk, both feet slid from under him and he fell on the left shoulder, striking the back of his head on the sidewalk with great force. This rendered him unconscious for about five minutes, and when he regained consciousness he was unable to move any of his limbs. This inability (motor) lasted for about half an hour, after which he slowly gained power, first in the legs and then in the right arm, but none returned in the left arm. As the man was unable to stand, the patrol was sent for and he was brought to the dispensary, where it was found that when he attempted to stand he would totter and fall if some one did not catch him. The patient stated that when he was trying to stand his back felt like a piece of paper, and it seemed to him that his spine was "*wabbling about.*" A rough test showed tactile sensation to be intact in all limbs, but practically no motor ability in the left arm. After remaining in the surgical ward for a short period, the patient was transferred to my care in the medical ward. His condition was as follows:

The patient had a marked deformity in the neck. The head was twisted to one side and slightly rotated, and the deformity was most prominent on the left side. With a finger in the pharynx the deformity could also be felt as a projecting mass on the posterior wall

of that cavity. The head was held in a very rigid and unnatural position, but there was no complaint of pain.

Motor Symptoms. The patient was paralyzed in the left upper extremity. He could not move the left arm at all, but he could flex and extend the forearm at the elbow. He could neither pronate nor supinate the forearm. He could flex and extend the thumb and index finger, but could not flex the middle, ring, or little finger; neither could he separate the fingers. The electric reaction in the affected muscles was not significant except in the deltoid and

FIG. 1.



Thermoanæsthesia and analgesia on the side opposite the paralysis of motion.

pectoralis, in which the faradic contractility was slightly diminished. There was no atrophy of the muscles, nor fibrillation. There was no paralysis in the left leg, a fact which is important, nor in the right arm or leg. There was no paralysis of the bladder or rectum. There was no involvement of the spinal accessory nerve, nor of the phrenic nerve, nor of any muscles of respiration. In fact, pressure symptoms were remarkable for their absence.

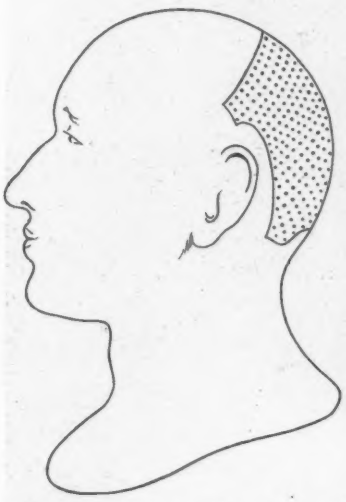
Sensory Symptoms. There was very marked loss of thermic sense in the *right* arm and forearm (that is, on the side opposite the motor

paralysis). The thermic sense was confused in the remaining parts of the right side, extending from the region of the fourth cervical vertebra. There was also analgesia of the entire *right* side from the region of the fourth cervical vertebra, also more pronounced in the arm and forearm.

Above the fourth cervical vertebra was an area one inch wide, which was hyperæsthetic; above this zone sensation shaded rapidly to normal.

There was no tactile anæsthesia anywhere, either on the left or right side. All these tests were made with great care, and sugges-

FIG. 2



Anæsthesia in the area of the great occipital nerve.

FIG. 3.

Case of dislocation of the atlas.

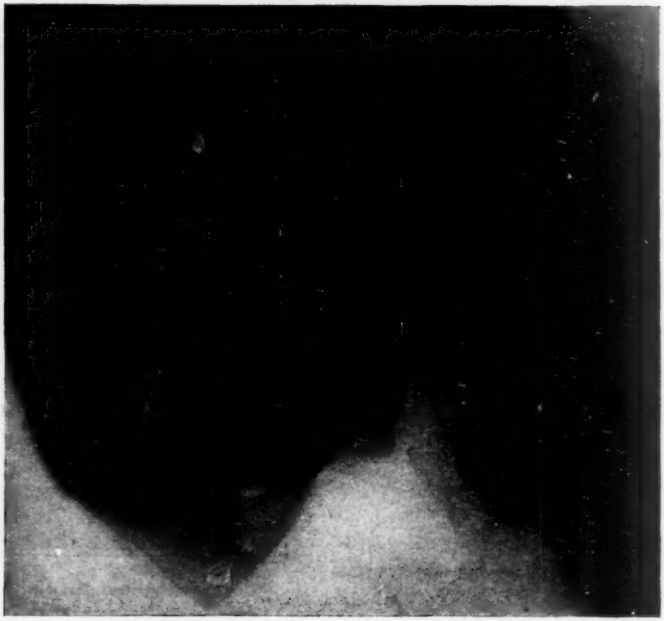
tion was avoided as much as possible. The patient never exhibited any of the stigmata of hysteria, and these sensory disturbances were not transferable. There remains, however, to note one sensory disturbance which may possibly be of great significance. This was a distinct area of tactile anæsthesia in the region of the distribution of the great occipital nerve of the left side. The great occipital nerve comes off from the second cervical nerve, and this second cervical nerve emerges from the spinal canal between the atlas and the axis. The involvement of this nerve, in view of what is shown by the skiagram, is significant, and is possibly the most important localizing symptom in the case.

The patient's sensory symptoms improved during his stay in the hospital, and eventually almost disappeared, but the motor paralysis in the left arm and forearm has persisted, and the deformity in the cervical region is unchanged.

The interpretation of the symptoms in this case has not seemed to me altogether easy.

The skiagram, which I exhibit, shows that the lesion is very high, and in fact the atlas appears to be displaced. The vertebræ below it, beginning with the axis, are in place, as is shown quite

FIG. 4.



Skiagram of dislocation of the atlas.

clearly by the relative positions of their spinous processes and by the distinctness of the intervertebral spaces. I have therefore taken the liberty of calling it a case of dislocation of the atlas, although I am fully aware that this is usually considered to be promptly fatal. Certainly it is difficult to conceive how the atlas can be dislocated and immediate pressure not occur on vital regions of the cord. But I call particular attention to the fact that displaced vertebræ can be felt in the pharynx, although by mere digital examination it is of course not possible to say what vertebra or vertebræ this may be. But

it must necessarily be high in the neck, for only the first four, possibly five, cervical vertebræ can be reached by a finger in the pharynx. A symptom of especial localizing value is the anæsthesia in the distribution of the great occipital nerve. This clearly indicates a high lesion, for the great occipital nerves are branches of the second pair of cervical nerves, and these pass out between the atlas and the axis.

The motor paralysis of the left arm alone is extremely difficult to account for. The brachial plexus passes off far below the apparent level of the lesion, and the fact that the leg is not involved shows

FIG. 5.

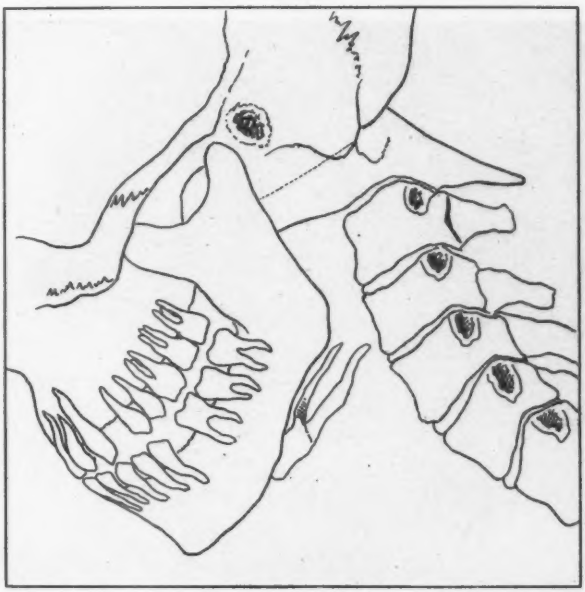


Diagram showing the tilting forward of the head in front of and slightly off of the vertebral column. The drawing is necessarily diagrammatic in the region of the atlas, as the details do not appear clearly in the skiagram.

that the arm paralysis is not due to pressure on the lateral tract. Again, the arm paralysis is of the peripheral type, as would be due to a lesion of the anterior nerve roots, for there is some muscular atrophy with faradic changes.

The sensory symptoms seem to indicate a very localized pressure on the anterolateral region; that the posterior columns are not involved is shown by the absence of tactile anæsthesia.

Dr. Walton, of Boston, has recently reported several cases of dislocation of the cervical vertebræ, and has very clearly pointed out their mechanism. A displacement of the articular surfaces of

two adjoining vertebræ, with only a slight forward dislocation of the bone on one side, can cause such a deformity as this patient has without much if any pressure on the cord. Such dislocations have been successfully reduced, and have even reduced themselves spontaneously during sleep or during ether anæsthesia. But in case of the atlas we have to reckon with the odontoid process of the axis. The query arises, Could this odontoid process be fractured and allow the atlas to slip? Finally, Can there be two lesions, one of the atlas and one lower in the spine involving the anterior roots, that go to

FIG. 6.

Skiagram of normal skull and spinal column.

form the brachial plexus? The fact that a dislocation of the atlas may occur, and the patient continue to live for weeks and even years, is proven by several well-authenticated cases. The following references are to some of these cases.

Handyside[1] described a case of *spontaneous* dislocation of the *processus dentatus*, with ankylosis of the upper part of the spine, and unattended with any symptom of paralysis. This case came on during a severe attack of rheumatic fever, and its causation was obscure. There was no caries. This man lived ten years and

[1] Edinburgh Medical Journal, 1840, vol. liii. p. 876.

worked at his forge. He died very suddenly with asphyxia. At the autopsy the right inferior articular surface of the atlas was found dislocated downward and forward over the corresponding articular surface of the axis, and ankylosed. There was also ankylosis of the occipital bone to the atlas. The spinal canal was reduced to a space measuring two lines in some diameters, and the lower part of the medulla oblongata was compressed.

Stanley[1] reported a case of long-standing ankylosis of the five superior cervical vertebræ, with dislocation of the atlas. The clinical

FIG. 7.

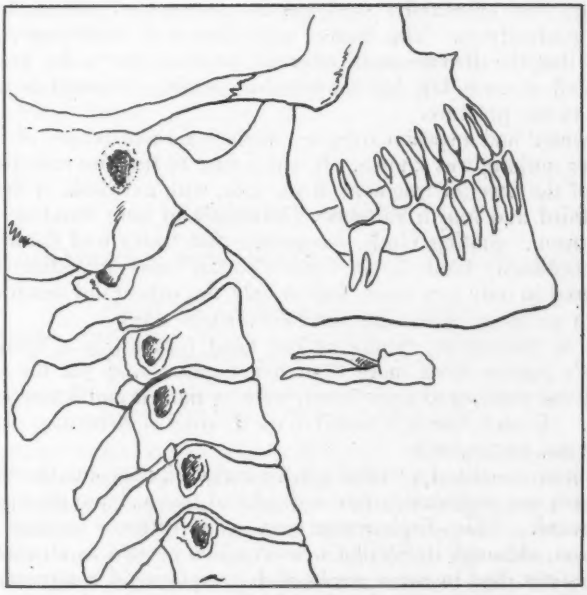


Diagram of the normal skull and spinal column in place.

history is obscure, but the patient was a sailor, who continued at his work. He died as the result of an accident, and the autopsy was carefully reported.

Debenham and Hutchinson[2] reported a most important case of a man who dislocated the atlas and sustained a fracture of the odontoid process of the axis, and yet lived two years. The diagnosis was confirmed by autopsy. The atlas with the included odontoid process was dislocated half an inch forward and a little to the left

[1] Edinburgh Medical Journal, 1839, vol. li. p. 563.
[2] Report of London Hospital, 1867, 1868, vol. iv. p. 210.

side. The odontoid process had been broken through the base, and was ankylosed to the atlas and to the front of the axis in its new position. The lower articular parts of the atlas, pushed forward and downward, were ankylosed to the front surfaces of the axis, and the axis and third vertebra were also ankylosed. The displacement of the atlas forward was such that its posterior arch crossed the spinal canal and left the greater part of the canal behind it. The portion of the canal in front and through which the cord passed did not admit the tip of a child's little finger. It measured the third of an inch from behind forward and three-quarters of an inch from side to side. The cord must have been much compressed. This patient was eventually paralyzed in motion and sensation, but only gradually so. The clinical report was very inadequate. It is likely that the displacement, after the original injury, did not take place all at once, but by degrees, thus leaving the cord to adjust itself to the pressure.

Wyman[1] had a specimen from a dissecting-room subject of whose history nothing was known. It was a case of fracture and dislocation of the anterior fragment of the axis, with ankylosis of the axis and third and fourth vertebræ. Evidently of long standing.

Stimson,[2] quoting Gurlt, recognizes that fracture of the atlas is not necessarily fatal, for in Gurlt's eleven cases immediate death occurred in only two cases, and in only two others did death occur within an hour. One case survived thirteen days.

As to *dislocation*, falling of the head forward is a symptom. Coste's patient lived more than five months, and yet the spinal canal was reduced to a slit 5 mm. wide on the left and 2 mm. on the right. (Coste's case is reported in the *Journal de Bordeaux*, August, 1852; not attainable.)

Stimson speaks of a "bilateral dislocation in opposite directions," in which one articular surface is displaced forward and the opposite backward. This displacement can exist without causing compression, although in Sédillot's case,[3] which is cited as an example, the patient died in seven weeks with symptoms of compression.

Phillips reports a case[4] in which the posterior arch of the atlas was broken off and remained in place, while the anterior portion, carrying with it the fractured odontoid process, was displaced so that it lay entirely in front of and became united with the body of the axis. The patient survived forty-seven weeks.

In Dubreuil's case the patient lived until the seventh day; in Gibson's case until the seventh day. Stimson calls attention to the falling forward of the chin on the chest, and to prominence in the pharynx, and deformity at the back of the neck.

Scudder[5] says that by palpation through the mouth the bodies

[1] Boston Medical and Surgical Journal, 1862, vol. lxv. p. 333.
[2] Fractures and Dislocations, 1899.
[3] Gaz. med., 1842, p. 776.
[4] Med. Chir. Trans., vol. xx. p. 78.
[5] Treatment of Fractures, Philadelphia, 1903.

of the cervical vertebræ may be felt as low as the fifth cervical vertebra. He also says that unilateral dislocation is the most common form, one articular process slipping over and in front of the one below. This causes the head to tilt and rotate.

The above cases do not by any means exhaust the literature of the subject, which is quite extensive, as may be seen by reference to the *Index Catalogue*. Most of the literature, however, refers to cases which have been immediately or quickly fatal, and these of course are the most common. I have thought it worth while merely to collect a few cases in which the patients have survived the accident for a comparatively long time.[1] The opinion that a dislocation of the atlas, as a result of accident, is necessarily quickly fatal, is thus seen to be erroneous. No reference has been made here to cases of caries of the bone, causing displacement, a quite well-known instance of which is related by Mr. Hilton in his treatise on *Rest and Pain*.

VENEREAL WARTS.

THEIR ETIOLOGY, PATHOLOGY, DIAGNOSIS, AND TREATMENT.

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(From the Pathological Laboratory of the College of Physicians and Surgeons and the Genito-urinary Clinic of Professor Charles F. Bevan.)

Various terms are in use to designate this pathological condition. A tolerable acquaintanceship with them may prove helpful to the student of venereal diseases. The following serve as examples: verrucæ venereæ; verrucæ of the penis; excrescences; warts; cutaneous tumors; papillomata; condylomata; sycomata; vegetations; venereal vegetations; papillary excrescences; papillary fibromas; acuminate warts; multiple pointed condylomata; *Feizwarzen* ("fig warts"); *Feuchtwarzen* ("moist warts").

The origin of these terms is not definitely known. However, it is fair to assume that the nature and character of the growths, as well as their common seat, gave to them "a local habitation and their name."

Definition. Moist or dry papillary overgrowths, varying in size and number, acuminate or flattened, sessile or pedunculated, appearing usually upon the mucocutaneous surfaces of the male and female genitalia. They are also found upon the scrotum, and

[1] Other references are: Shaw, Med. Chir. Trans., vol. xxxi. p. 289; Lawrence, ibid., vol. xiii. p. 387.

occasionally around the anus. On mucous surfaces they are moist; on skin surfaces they are dry. They are almost invariably multiple, and they may be either venereal or non-venereal.

HISTORICAL NOTE. Venereal warts are not mentioned in the genuine works of Hippocrates. Liston, as well as Celsus, describes them minutely. John Hunter believed them to be syphilitic in origin. In Van Buren and Keyes' first book—the pioneer work on this subject—venereal warts are given due consideration. In the older works on surgery they are often described as a manifestation of syphilis.

FIG. 1.

Large, multiple condylomata acuminata ("papillofibromata") of the human penis; sessile, confluent, and completely filling the coronary sulcus, forming a so-called "collarette." The glans penis is free from growths, and a large drop of gonorrhœal pus is seen oozing from the meatus. Even the keratinized acicular tips of the growths are recognizable and appear of a darker shade than the surrounding tissues. (Photograph by Dr. John S. Fulton.)

OCCURRENCE AND FREQUENCY. Age is no factor in the production of venereal warts. They are frequent in children and in pregnant women suffering from irritating discharges—urethral or vaginal. They occur oftenest, however, in young adults of either sex, ranging in age from fifteen to twenty-five years. In the subjoined lists the youngest is fifteen, the oldest thirty-eight.

In males, though they are largely subpreputial—the mucous surface of the prepuce, the coronal sulcus, and sulci of the frenum being their favorite seats—they may occur anywhere on the preputial fold. Warts are also encountered on the surface of the glans and less frequently upon the lips of the meatus. According to Valentine, "they begin in the sulci at either side of the frenum and in the sulcus behind the corona with equal frequency." As stated above, they are also found, though rarely, upon the scrotum and about the anus.

FIG. 2.

Human penis, showing multiple pointed condylomata, aggregated into large masses, pedunculated and springing from the coronary sulcus, as in Fig. 1. A few isolated warts are also seen scattered over the mucous lining of the prepuce. The surfaces of the tumor-masses have lost their cauliflower-like appearance because of compression by the foreskin. (Photograph by Dr. John S. Fulton and Mr. John Johns.)

In the female they originate at the entrance of the vulva, on the carunculæ myrtiformes, the nymphæ, the fourchette, at the introitus vaginæ, at the meatus urinarius, on the skin of the perineum and around the anus. Keyes, in his recent book, states that "venereal warts are found in greatest luxuriance within and around the vulvæ of pregnant women affected with irritating discharges—discharges not necessarily venereal in any sense."

In either sex they may be situated in the urethra and inferior part of the rectum. Oberländer describes a condition of papillomatous

urethritis. Like subpreputial warts, these intraurethral growths vary greatly in size and number. There may be a few near the meatus, or many sprinkled along deeper in the canal. Since the introduction of the urethroscope urethral vegetations have been shown to be not so rare as was formerly believed. They may be sessile or pedunculated and grow from any portion of the canal, but their commonest seat is in the navicular fossa and behind strictured portions of the urethra, springing from the floor. They may attain a size sufficient to obstruct the outflow of urine. Usually, however, they are small and occur in the first inch of the urethra. John Hunter, in all his examinations of dead bodies, saw only two instances of intraurethral papillomata, and these were in very old strictures, where the urethra had suffered considerably. Hunter made the assertion that he had never met with urethral vegetations in women, whilst Ricord said that they are more common in women than in men.

Acuminate condylomata abound around the anus in anorectal gonorrhœa and in untidy females who allow the parts to reek with acrid secretions and irritating discharges. In the appended list of eighteen cases of venereal warts occurring in the out-patient department of the City Hospital there is one example of condylomata of the anus. In this instance—that of a male negro—the rectum was funnel-shaped and there was a slight grayish-white issue, but the gonococcus was not demonstrated.

As to the frequency of venereal warts there is a dearth of statistical evidence bearing upon this point. In the most recent 1800 cases of venereal diseases treated in the out-patient department of the City Hospital, under the supervision of Dr. A. Samuels, venereal warts occur eighteen times or in 1 per cent. of the cases. This, I think, is placing the estimate a little too low. Two per cent. would probably be more nearly correct. An epitome of these cases may be appreciated. Only the salient points are presented. (See Table I.)

Occurrence in Animals. Papilloma of the penis is not restricted to man. It occurs in the equine family, notably the horse. Ruminants are peculiarly exempt. In horses it takes on more closely the character of a true wart of the skin or mucous membrane. I have seen it a number of times. These papillomatous projections are usually observed on the inner surface of the sheath, on the foreskin, and behind the glans—oftenest, however, on the upper and inner surface of the sheath. They are largely due to uncleanness and excessive moisture resultant from neglect on the part of the farrier. They are usually sessile, and occur as a rule in clusters or groups resembling, on a small scale, the "corymbose" variety of smallpox. Youatt, in his excellent treatise on *The Horse*, thus describes them: "These (warts) are tumors of variable size, arising from the cuticle, and afterward connected with the true skin by

means of the vessels which supply the growth of the tumors. They are found . . . on the penis and the prepuce." Left alone and neglected, condylomata about the sheath or penis of the horse sometimes become carcinomatous during the age of physiological decline. At least one such instance has come under my observation. So far as I know, papillary growths of the penis are not found in other of our domesticated animals. Dogs, however, are subject to them. Ashmont says: "Not infrequently as the result of balanitis, warts or vegetations appear on the genitals of dogs. Other causes have been assigned, but in this situation they are doubtless induced by irritating discharges. They may exist as a single excrescence or as a group of several united."

ETIOLOGY. The causes of venereal warts are predisposing and exciting. The most important predisposing cause is a long, tight foreskin. Some persons exhibit a constitutional tendency toward these warts. Uncleanliness and maceration of their seat, the presence of an irritating discharge, and balanoposthitis are the usual exciting causes.

Hunter believed in the specificity of venereal warts. Ricord dissented and said: "As to the special cause which excites and keeps up these vegetations, it cannot be sought for in the virus of syphilis." Modern authorities hold to the opinion that the determining factors in the production of venereal warts are uncleanliness and irritation, as in gonorrhœa or balanitis. In persons suffering from herpes præputialis or chancroid they are by no means uncommon. Certain it is that an elongated, phimotic prepuce, replete with retained and decomposing secretions, furnishes an ideal field for the development and growth of these papillary excrescences; and the combined influence of uncleanliness and the irritation produced by a gonorrhœal discharge is the usual *raison d'etre*. Of the eighteen cases of venereal warts (see Table I.) treated in the out-patient department of the City Hospital, seven, or nearly 40 per cent., showed no evidence of venereal disease, while the remaining 60 per cent. were directly traceable to it. The classification of these latter cases is as follows: complicating gonorrhœa, 4; chancroidal ulceration present, 2; chancre and phimosis, 1; history of syphilis, 1; herpes præputialis, 1; suppurating bubo, 1; proctitis (warts of anus), 1. The case listed as occurring with "suppurating bubo" probably should have been placed in the first category—the non-venereal cases. The patient, a young negro above the average intelligence of his race and a medical student, emphatically stated that he never had had any venereal disease and that the warty growths were the cause, *and not the effect*, of the suppurative lymphadenitis. To recapitulate: In each of the non-venereal cases the foreskin was redundant and tight, and the glans was thus kept in an unduly moist state. In the venereal cases it is to be noted that an irritating discharge, gonorrhœal or other, was either present or had

existed at a time coeval with the first appearance of the warty growths. They may be caused, though rarely, by prolonged contact with secretions emanating from mucous patches within the cavity of the prepuce.

Quite recently in my private work there occurred five cases of venereal warts. Three were complications of gonorrhœa, while in the others there was no history of venereal disease. In one of the cases the warts, varying greatly in size, were very numerous, abounding at the meatus, on the glans penis, upon the mucous and cutaneous surfaces of the prepuce and within its cavity, in the coronary sulcus, and in the sulci of the frenum. In three of the cases the warts were few in number and occurred in the sulci of the frenum. In the fifth case the warts, numbering but three, were located on the mucous surface of the prepuce. Table II. is a tabulation of these cases.

So far as is definitely known, venereal warts are neither infectious nor contagious. Ricord says: "The assertion that they are contagious, advanced by some persons, is false." White and Martin, than whom there are no greater authorities, say: "Proof as to the contagious nature of discharges from venereal warts is still wanting, though there are many recorded cases of condylomata developing apparently as the result of contagion." The clearest and best exposition of this phase of the subject is that by Taylor in his *magnum opus*. He mentions the following seemingly convincing instances: Güntz, of Dresden, reported the case of a child who contracted these growths from having used repeatedly the same chamber as its nurse, upon whose genitals at the time innumerable vegetations were seated, and quotes the so-called successful vaccinations of Dr. Kranz in Lindwurm's clinic. Güntz further quotes the case of Sir Astley Cooper's assistant, who, during the ablation of a large condylomatous growth, was wounded in the vicinity of the fingernail. As a result there was developed at the point of injury a growth of condylomata acuminata. In six experiments conducted by Güntz himself, vegetations were removed from the genitals and placed in incisions on the arms, in each instance with a negative result. The late Prof. Petters was the chief opponent of the doctrine of the contagiousness of venereal warts. His exhaustive essay contains the details of twelve carefully conducted but negative experiments. Taylor summarizes thus: Hebra disbelieved in the contagiousness of these lesions, and Ricord was of the same mind. Reder considers the contagion probable, while Geigel regarded it as certain. Zeissl admitted their contagiousness, and Neumann, while conceding the possibility, was in doubt. Lebert, on the contrary, gives it as his opinion that these growths are positively not contagious.

Oberländer does not believe that pointed warts under the prepuce or in the urethra are due to gonorrhœal infection, yet he does consider them contagious. The late Professor Rohé considered their origin by contagion as probable, but not absolutely demonstrated.

To conclude: Concerning the etiology of condylomata it may be said that a long foreskin is the most frequent and most important predisposing cause. Uncleanliness and undue moisture, combined with an acrid, irritating discharge—usually gonorrhœal—are the exciting causative factors in 60 per cent. of the cases; the remainder, 40 per cent., are non-venereal and are due to uncleanliness and maceration of their seat alone. They are essentially inflammatory. The frequent presence of a balanoposthitis or its history, as well as the microscopy of the growths themselves, is, I think, incontrovertible proof of the truthfulness of this statement. The question as to their infectious or contagious nature is still *sub judice*.

Pathology and Histopathology. Condylomata, when small, appear as hyaline spots, often highly vascular and composed largely of epithelium. They may be discrete or confluent, sessile or pedunculated, single or branched. Viewed grossly, they may be cauliflower-like in appearance or form aggregations resembling a cock's comb. Their delicate structure, as well as their exposed situation, renders them extremely liable to injury, and on account of their excessive vascularity they are prone to bleed profusely on the slightest provocation.

Histopathologically, venereal warts are true papillomata. They consist of a framework of connective tissue covered by stratified epithelium. The connective-tissue stroma is quite vascular, and the epithelium usually of the squamous type. They are due to "hypertrophy of the papillary and mucous layers of the skin; at the same time there is a corresponding development of bloodvessels." Papillomata are of two kinds—epithelial and fibrous—and, as Guiteras says: "It is frequently impossible, owing to coincident hyperplasia of the connective tissue, to separate epithelial from fibrous papillomata. Many papillomata are inflammatory, and are best classified as *hypertrophies*, being due to irritation."

One of the earliest descriptions of the histology of venereal warts is that by M. Lebert. He speaks of them as "nothing else than a development of the papillæ of the epidermis." Hunter and Ricord describe them minutely; likewise Virchow in his *Cellular Pathology*. Weichselbaum, quoted by Valentine, described a condylomatous excrescence as a "simple or branched papilla, built on the type of a skin or mucous papilla, and covered with epithelium of varying thickness. The connective tissue in these papillæ is generally much richer in cells and vessels than is the connective tissue of the base from which they spring. The epithelial covering can be materially thicker than that of the region from which it originates, but ordinarily it has the usual character of the epithelium of the region. The papillomata proceed from normal papillæ of the skin or mucosa, which enlarge; new formation of papillæ also takes place."

Unna does not regard condylomata as true papillomata, and contradicts the latter statement of Weichselbaum, inasmuch as he says

there is not any independent growth of the papilla in condylomata, but only an increase of their size from infiltration with leukocytes. To the infolding of the proliferating epithelium upon the papillæ, Unna attributes the apparent increase in their number.

Stengel, Green, Delafield, and Prudden, and other recent pathologists, describe condylomata—"venereal warts." Delafield and Prudden define them as "hypertrophied papillæ covered with epithelium."

The writer has studied carefully numerous microscopic sections of venereal warts, cut in divers directions and from different parts of the growths, and stained by a number of the most approved meth-

FIG. 3.

Microscopic section of "papillofibroma" of human penis, shown in its entirety. At the lower left-hand margin may be seen a small area of normal skin—truly a striking contrast. In close proximity to the outskirts of the specimen are tips of papillæ, cut transversely. The acuminate extremities of the subdivisions of the growth stand out in bold relief, and the vessels of the corium are congested. The surface-layers of epithelium have undergone keratohyaline degeneration. The structure is epithelial and fibrous tissues in almost equal proportions. × 23. (Photomicrograph by Dr. John S. Fulton and Mr. John Johns.)

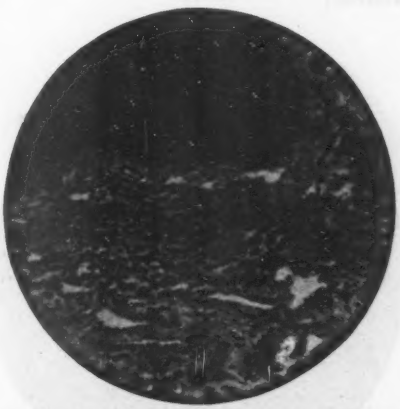
ods. A detailed account of the most striking results obtained, arranged under two headings, "Tissue Stains" and "Bacterial Stains," will next be given:

1. *Tissue Stains.* (*a*) Stained in the regulation way with eosinated logwood, it is next to impossible to conceive of a more beautiful picture in pathological histology. The epithelial and fibrous strata seem about equally divided, and between the two there is a zone rich in adenoid tissue and resembling histologically the basement membrane of the stomach mucosa. The relation between stroma and epithelium can be seen even with the naked eye. Seen in its entirety with a very low-power lens (Fig. 3), the contour of a typical branch of one of these growths is not unlike that of a normal papilla of the skin or tongue.

Epithelium. Under the low power the most striking change consists in a perceptible thickening of the epithelium, which seems to

affect all of the strata equally. The papillæ and the interpapillary connective tissue show a great increase in length and thickness. That portion of the corium adjacent to the deepest layer of epithelium shows a distinct zone of cellular infiltration, and the vessels of the corium show some congestion. Under a higher power the thickening of the epithelial layer seems to be due, at least in part, to actual increase in size of the individual epithelial cells. This is especially noticeable in the prickle-cell layer of the rete Malpighii, a condition first described by Dürck and later observed independently by the present writer. Here the nuclei are swollen and often surrounded by a clear, œdematous vacuole and the cytoplasm is also swollen and at times pale and œdematous.

FIG. 4.



Microscopic section of "papillofibroma" of human penis. There is a pretty sharp line of demarcation between the epithelial covering and the connective-tissue framework. A layer rich in cells and resembling lymphoid tissue is seen immediately beneath the deepest layers of epithelium. At no place has the epithelium invaded the connective tissue—a point to be borne in mind in differentiating from epithelial carcinoma. × 745. (Photomicrograph by Dr. John S. Fulton and Mr. John Johns.)

There are certain cells in this region which almost resemble parasites. These are about the size of a red blood corpuscle, possess small round or elongated, darkly staining, often irregular nuclei, and are surrounded either by a clear vacuole or by a minimal amount of eosin-staining protoplasm. In addition to hypertrophy of the individual cells there is also evidence of hyperplasia or numerical increase. This is proven by the presence of a moderate number of karyokinetic figures indicating rapid multiplication by indirect cellular division.

Corium. The intercellular lymph spaces are distended by cells of various types. There are a few polynuclear leukocytes present, but the exudation is mainly made up of small mononuclears or

lymphocytes and proliferated endothelial cells. This cell accumulation is particularly marked at the bases of the papillæ, in the perivascular lymph spaces surrounding small nerves. There are also present a few large lymphocytes or "highly vacuolated plasma cells of Waldeyer."

(*b*) With Van Gieson's stain the connective tissue of the corium is well shown, and it can be traced as fine strands into the connective tissue of and between the papillæ.

(*c*) Sections stained in polychrome methylene blue (Unna's) show a number of plasma cells, but no *mastzellen*. These cells, described by Unna and occurring in subacute and chronic inflammatory processes, are not identical with the plasma cell of Waldeyer alluded to above. The protoplasm stains violet blue and there are no distinct granules.

FIG. 5

Section of "papillofibroma" of human penis stained by the Gram-Weigert method. Bacteria (cocci, diplococci, and bacilli) are demonstrable lying in and among the epithelial cells. Darkly-staining plasma cells and a limited number of leukocytes are seen in the peripheral portion of the corium. × 1000. (Photomicrograph by Mr. John Johns.)

2. *Bacterial Stains.* Sections of specimens of venereal warts hardened in alcohol were next stained for bacteria. The methods employed are: Gram's, Gram-Weigert's, Stokes' modification of Gram-Weigert's, and the tubercle-bacillus method.

(*a*) *The Gram Method.* Large numbers of Gram-staining bacteria—cocci, diplococci, and bacilli—are to be seen. These will be described in the succeeding paragraphs.

(*b*) *The Gram-Weigert Method.* On staining sections by Weigert's method, masses of bacteria could be seen, even under the low power. These bacteria are limited to the stratum corneum or

scaly layer of the epidermis, and cannot be found in the adjacent stratum lucidum or granulosum. Under the oil-immersion lens they consist mainly of micrococci and diplococci, but a few fine, long bacilli can also be distinguished. These bacteria are strictly limited to the surface and do not invade the deeper layers of the epidermis. They seem to be distributed in greater or lesser numbers throughout the entire superficial horny layer of the skin.

(*c*) *Stokes' Method.* This is a modification of the Gram-Weigert method. It was first described by Dr. William Royal Stokes in his paper on "Ulcer of the Stomach Caused by the Diphtheria Bacillus," published in the *Johns Hopkins Hospital Bulletin*, July, 1901. The preliminary staining with hæmatoxylin has been dispensed

FIG. 6.

Magnification and specimen same as in Fig. 5, showing numerous micrococci and bacilli in the superficial layers of the epidermis. × 1000. (Photomicrograph by Mr. John Johns.)

with, and the method now simply consists in first staining the section in 1 per cent. watery eosin, and then decolorizing with water. The section is then stained by the usual Weigert method.

When the sections are stained by Stokes' modification of Weigert's method, similar bacteria to those described above can be made out. This process serves as a good histological stain as well as a bacterial stain, and in my experience has given better results in routine work than the preliminary staining with carmine.

A method almost identical with the above has been used quite extensively in the Pathological Division of the Bureau of Animal Industry, United States Department of Agriculture. In this well-organized department, bacteria as well as sections of tissue are not infrequently stained by Gram's method, or Gram-Weigert's method,

and followed by, or counterstained with, eosin. In Stokes' modification the staining with an aqueous solution of eosin precedes the Gram-Weigert method.

(*d*) *The Tubercle-bacillus Method.* No bacteria were demonstrable in sections stained by the Ziehl-Neelson-Gabbett method.

Histopathology of Papilloma of Horse's Penis. The changes in the epithelium do not differ materially from those described above in the human cases, but the cellular infiltration of the corium presents a complex study. In the first place, the tissue is richly infiltrated with proliferated, elongated connective-tissue cells; but, in addition to this, there are greatly increased numbers of large and

FIG. 7.

Papilloma from the penis of a horse, showing the hyperplasia producing great elongation of the papillæ and the loose fibrous tissue of the corium beneath. The upper portion of the photomicrograph shows a sulcus containing many exfoliated superficial epithelial cells. × 23. (Photomicrograph by Mr. John Johns.)

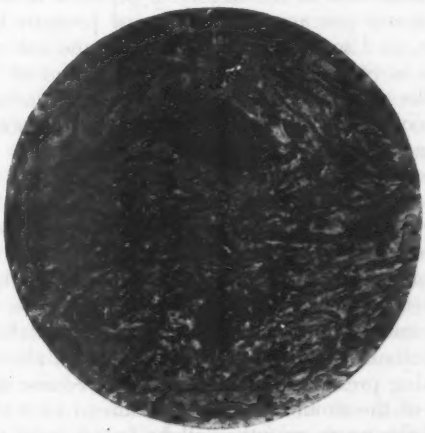
small lymphocytes. The large lymphocytes often have their nuclei eccentrically placed, resembling the so-called plasma cells. Both the large and small lymphocytes are found in excessive numbers in the lymphatic spaces and in the capillaries, and they doubtless wander from the bloodvessels into the surrounding tissues. The crowded condition of the lymphatics is probably due to the absorption of these cellular elements from the tissues. There are a few eosinophiles scattered through the corium. The corium presents a rather loose, myxomatous appearance, and the lymph spaces are often perceptibly distended. The interpapillary connective tissue—of which the papillæ of the true skin is a physiological prototype—contains many large and small lymphocytes.

SYMPTOMATOLOGY. There is no definite symptomatology peculiar to venereal warts. The patient may complain of a disagreeable

sensation—a sense of "fulness"—or a feeling of discomfort about the parts, and much smegma and a peculiar, sickening odor are usually in evidence, especially when the warts are very numerous. Unless infection, with subsequent ulceration, takes place, these warty growths are attended with but little, if any, pain. Even when acutely or subacutely inflamed, pain is not a prominent symptom. Specimens from one of my cases show a subacute inflammatory process; yet there was no pain connected with it.

In women condylomata give rise to "itching, burning, and a general feeling of discomfort, but otherwise do not cause symptoms." Stoner reports a case in which numerous condylomata

FIG. 8.



Specimen same as Fig. 7. This picture shows the myxomatous fibrous tissue which forms the base of the tumor. The connective-tissue cells, with their wavy distal filaments, are well shown. The lymphatic capillary contains numerous lymphocytes, which are also scattered throughout the tissue as so-called plasma cells. A capillary bloodvessel, filled with red blood cells and containing a few lymphocytes, is also seen in the upper portion of the picture. × 745. (Photomicrograph by Mr. John Johns.)

studded the surface of the vulva and vaginal walls, a large mass occupied a site adjacent to the anus, and several occupied the cervix uteri. A profuse gonorrhœal discharge from the vagina and urethra was present, but there were no subjective symptoms. I have seen an analogous case. Excluding the mechanical inconvenience, the affection was symptomless and painless.

The symptoms of intraurethral papillomata next merit brief discussion. These are usually slight. There is a thin, mucopurulent discharge, chronic from the first, with slight burning during urination. When they attain large size, or grow upon the meatus, they may interfere with urination and ejaculation. Often there is free bleeding on instrumentation.

Morrow, in a recent article on "Growths of the Male Urethra," says: "Symptoms depend somewhat on the size and location of the growths, those of the anterior urethra producing points of tenderness, gleety discharge, obstruction, and urethral hemorrhage; in the posterior urethra they cause hæmaturia, urethral hemorrhage, sexual hyperæsthesia, prostatic enlargement, frequent micturition, incontinence, and obstruction."

DIAGNOSIS. (*General and Differential.*) By simple inspection the diagnosis of venereal warts can usually be established beyond peradventure. Papillary excrescences, cauliflower-like and appearing on the moist mucocutaneous surfaces of the external genitalia of young persons of either sex, are almost invariably *verrucæ venereæ*. An impure connection or the history or presence of a venereal disorder is not a *sine qua non*. By reason of pressure inflicted by a tight foreskin, and sometimes as a result of the use of cauterants, their exterior is very materially altered. Instead of their pristine cauliflower-like appearance they become much flattened, coarser, and denser looking. Even then the history, seat, and mushroom-like appearance of the growths are almost certainly sufficient for their intelligent identification.

The diagnosis of intraurethral papillomata is made by distending the meatus with the thumb and finger, when one or more warts may usually be seen at or just within the meatus. When more deeply seated, the endoscope and bulbous bougie are valuable diagnostic aids. The tendency of these growths to bleed on the slightest touch compromises the usefulness of the endoscopic tube. By deeply inserting a bulbous bougie of fair size and with shouldered acorn tip, and making pressure externally over the course of the urethra just in front of the shoulder of the instrument as it is withdrawn, fragments of the warty growths will be found upon this shoulder, and hemorrhage from the urethra will follow (Keyes).

For the sake of perspicuity I shall make brief allusion to the principal conditions from which *verrucæ venereæ* must be distinguished. These are: "condylomata lata," or syphilitic warts, epithelioma, mucous patches, urethral polyps and urethral caruncle when occurring in the urethral canal, and hemorrhoidal tumors when found about the anus or rectum.

In condylomata lata, or syphilitic warts, other manifestations of the disease are present, and a history of syphilis can usually be elicited. Only in long-standing cases, in which the external appearance of the warts is altered—when they are broadened by growth—is such an error in diagnosis likely to be made.

Epithelioma in its incipiency may be mistaken for condyloma. The patient's age, the presence or absence of infiltration of the base of the tumor, or tumors, and the surrounding tissues, and the condition of the neighboring lymph nodes are the most important differential points. The former—epithelioma—appears late in life and

is accompanied by infiltration of the surrounding tissues and involvement of the anatomically related lymph glands; in the latter—condyloma—these features are conspicuous by their absence, excepting as rare complications. However, as a precautionary measure, a wart appearing on the penis after middle life should be excised and subjected to careful scrutiny by a competent pathologist and microscopist.

Condylomata may be confounded with mucous patches. This can only occur when the former are flattened and macerated by free secretion or discharge. A history of lues, the pearly lustre of the mucous plaques, and the concomitant symptoms determine the diagnosis.

Differentiation from polypoid growths of the urethra and from urethral caruncle is of but slight import, as the treatment of these conditions is similar, namely, surgical removal. In condylomata, as previously stated, the urethroscope is of but little avail, because of the hemorrhage which ensues. Condylomata here as elsewhere are almost invariably multiple and are found oftenest in the anterior urethra. In one of Morrow's cases "twenty were removed by the snare, one came away spontaneously, and an interminable number were removed by the caustic solutions." Polypi—fibrous and mucous—are usually single and occur, as a rule, in the posterior portion of the urethra. They are not nearly so vascular nor sensitive as the multiple pointed condylomata. To employ the phraseology of Keyes, urethral polyps "do not bleed on contact with an exploring instrument, their only symptom being a slight urethral discharge and perhaps diminution in the size of the urinary stream, with some real or fancied urethral neuralgia."

Urethral caruncle is almost unknown in the male urethra. In the female it produces painful micturition—sometimes excessively so—vaginismus, and dyspareunia. Urethral caruncle is situated at the edge of the urethral mucous membrane and is slightly elevated above the surface. It is deep red in color, granular in appearance, and exquisitely sensitive. "Urethral polypus is non-sensitive, has a longer pedicle, and is usually attached higher up in the urethra" (Davenport).

Condylomata abounding about the anus and in the lower part of the rectum as a result of anorectal gonorrhœa may be confused with hemorrhoids. The differential diagnosis, however, is quite simple. "Hemorrhoids are either round, pendent tumors, or loose folds of the integument, having a smooth surface; whereas condylomata are flat and possess an irregular, warty appearance" (Agnew).

Prognosis. The prognosis as to the early disappearance of the warts is good. Regarding permanency of cure it must be said that recurrences are not infrequent. Unless the exciting cause be removed, the warts are extremely likely to return, and often more abundant than at first. Thorough eradication of the growths

themselves, and cauterization of their base, combined with removal of the etiological factor or factors, are the only measures that afford lasting relief. However, I cannot speak definitely regarding the frequency of return of these growths, nor are statistics relative to this point at my command. In Table I. there are chronicled three recurrences—a proportion of $\frac{1}{6}$ or $16\frac{2}{3}$ per cent.

The prognosis of intraurethral papillomata is unfavorable. Keyes states that "the malady may last indefinitely, individual warts disappearing to be replaced by others." Oberländer cites a case of warts in the urethra of a patient who had had a discharge for twenty years.

Complications and Sequelæ. Phimosis, paraphimosis, balanitis, and balanoposthitis are the commonest complications. Oftentimes, however, these conditions are due to the gonorrhœa which has caused the warts rather than to the presence of the warts themselves. As stated in a previous paragraph, a balanitis or a balanoposthitis is, in 40 per cent. of the cases, a forerunner and not a consequence of a crop of venereal warts. Inflammatory bubo, either suppurative or non-suppurative, sometimes results. Case XV., Table I., is an example of suppurating bubo complicating warts. Occasionally warts themselves become infected and undergo suppuration and ulceration. Even gangrene is a possible complication. Both Valentine and Taylor speak of it. A young man with a very prolific growth of warts of the penis, complicated by a paraphimosis, suppuration of the warty growths themselves, and a gangrenous area on the under surface of the constricted portion of the foreskin, was quite recently exhibited at Professor Bevan's clinic. He had suffered a severe and prolonged attack of gonorrhœal urethritis, and some discharge was still present.

Perforation of the prepuce sometimes results. Taylor mentions it. I have seen it once. Three years ago a middle-aged man was admitted to the surgical ward of the City Hospital with a fractured femur. He had an old healed perforation of the prepuce of considerable size, which he informed me resulted from sloughing of warts which he had had when a young man. In Morrow's intraurethral cases their presence produced dilatation of the urethra and prostatic enlargement. Anon they engender a chronic urethritis, and Hunter speaks of stricture being caused by them.

Malignant degeneration—the implacable aftermath of so many tumors primarily benign—may take place in persons beyond middle life, but such a consequence must be exceptionally rare. In two cases of epithelioma of the vulva with which I was conversant, the probable history in each case was that of long-standing condylomatous excrescences which had become malignant. Keyes amplifies the foregoing when he says that "warts and chronic balanitis are the most fruitful sources of epithelioma, the former especially if neglected and allowed to remain foul and moist." Kaufmann,

quoted by Keyes, collected thirty-three cases of epithelioma of the penis. Twenty-nine of the thirty-three began as apparently benign warts.

According to Keyes, implantation warts—warts occurring after circumcision—are especially liable to hypertrophy and become horns. Sterility, due to organic impotence, may result, the warts acting as a mechanical impediment to the performance of coitus.

PROPHYLAXIS AND TREATMENT. The prophylaxis and initial treatment of venereal warts are to all intents and purposes one and the same. In either instance, after cleanliness, the golden rule is, *remove the cause.* If a gonorrhœa exists, treat it by the latest and best methods. If there be a long foreskin, with accumulation of secretions, circumcise. If phimosis is present, a dorsal incision may be necessary. If a balanitis or a balanoposthitis, repeated cleansing and drying of the parts should be enjoined. These, combined with the intelligent use of some simple dusting powder, will generally be all-sufficient.

The treatment proper of venereal warts may be either medical or surgical. The former includes topical applications of the various dusting powders, ointments, lotions, pastes, and caustics. The second resolves itself into complete riddance of the parts of growths by means of the knife, scissors, or curette—preferably the scissors or the sharp spoon. Perhaps the use of caustic agents should be placed also under this caption.

As a preliminary measure it is expedient that we resort to medical or palliative treatment. The first principles—cleanliness, dryness and removal of the cause—having been faithfully complied with, one of the much-vaunted remedies—and their name is legion—should be employed. The relative merits of these subsequently will be discussed briefly *seriatim.*

Ricord wrote: "At the present day the rational course to take consists in treating the complications, *when such really exist,* and in making local applications to the vegetations as to a local disease. . . . Swediaur's powder is generally inefficacious. We should, in most cases, resort to cauterization, and especially to excision."

Medical Treatment. Dusting with calomel alone is one of the simplest methods of treatment. A dry dusting powder composed of calomel and bismuth—calomel one part, bismuth two parts—will perhaps be more efficacious. A formula in pretty general use in the routine treatment of this class of cases at the out-patient department of the City Hospital is:

℞.—Hydrargyri chloridi mitis . . . . . 1 drachm.
Bismuthi subnitratis . . . . . 2 drachms.—M.
Sig.—Dusting powder.

Dusting the growths with boric acid not infrequently causes their rapid disappearance. Zinc oxide and bismuth, equal parts, has its advocates. A 10 per cent. salicylic acid ointment may prove useful.

Resorcin sometimes supersedes all other local applications. It is thus prescribed at the hospital clinic:

℞.—Resorcini . . . . . 15 grains.
Vaselini . . . . . 1 ounce.—M.
Ft. ungt. Sig.—Locally, after carefully cleansing the parts.

The following mixture is recommended by White and Martin, and a similar one by Keyes:

℞.—Acidi salicylici . . . . . 1 drachm.
Acidi acetici . . . . . 1 ounce.—M.
Sig.—Apply with a brush once daily.

This combination forms a curd-like mixture and will generally remove warts within twelve to twenty-four hours. A sufficient quantity of the dregs should be deposited upon the growths to cover their entire surface, and allowed to dry. One or two applications are usually sufficient. Relapse is said not to occur after this treatment.

In the acuminate form, cleansing, drying, and dusting with powdered savin acts as a direct specific (Posner). Valentine recommends that the mass be touched three times daily with ferric chloride. The shrunken, shrivelled portions should then be curetted and the application repeated, until the base is reached. This must be thoroughly curetted and its bleeding arrested with cotton pledgets soaked in 5 per cent. solution of antipyrin.

Surgical Treatment. Surgical removal of the growths—curettement, extirpation, or excision—undoubtedly furnishes greater assurance of permanent success. This may be effected, as stated above, by means of the curette, knife, or curved scissors.

Neither curettement nor excision is as effectual as removal with the curved scissors. The first, because of its inaccuracy and incompleteness, and the second, by reason of its unhandiness, is to be superseded by a pair of rat-tooth forceps and curved scissors.

Unless the growths are very small and few in number, an anæsthetic, general or local, will be required. Ether, undoubtedly, is the safest and best general anæsthetic. Of the local anæsthetizing agents, ethyl chloride and cocaine stand ahead of all others. Ethyl chloride may be purchased in metallic containers ready for use, and is sprayed over the surface to be anæsthetized. Cocaine, in 10 per cent. solution, is always available and will answer every purpose.

The method of operating on condylomata is as follows: After a thorough cleansing of the diseased area, a 10 per cent. solution of cocaine is applied for five minutes before the operation. When the growths are discrete and small, they are seized, one by one, with a pair of rat-tooth forceps, drawn upward and removed, together with the underlying tissues, by a snip of the scissors. The bleeding points are then cocainized, touched lightly with pure carbolic acid, and dusted with iodoform or some other powder. The application of a gauze bandage completes the dressing.

When the neoplasm has a large base, or is confluent, the projecting mass may be shaved off level with the surrounding surface by means of a sharp, flat knife. The base should be thoroughly curetted, and then cauterized with carbolic or nitric acid. The wound is then dusted with iodoform or with a powder made of calomel and zinc oxide, equal parts of each, and a gauze dressing applied. As in the case of the smaller growths, the bleeding surface should be cocainized prior to cauterization, to render the operation painless. Bleeding, though free for a few moments, usually stops on cauterization, or on the application of a cotton pledget soaked in a 5 per cent. solution of antipyrin. In excising unusually large papillomata the hemorrhage is sometimes alarming. It is well, on such an occasion, to have an actual cautery ready for use in case of emergency. Only spouting vessels should be ligated.

When practicable, a still more radical step consists in cutting away the papilloma and its base entire, approximating the edges of the wound and suturing them. This operation is applicable when the growth, or growths, spring from the prepuce or skin surface.

Treatment with Caustics. The cauterant remedies usually applied are (*a*) nitric acid; (*b*) chromic acid; (*c*) caustic potash; (*d*) silver nitrate; (*e*) carbolic acid; and (*f*) glacial acetic acid.

When nitric acid is the agent employed, the surrounding parts should be protected by some bland ointment, the acid well rubbed in, and an antiseptic dressing applied. The application should be repeated on alternate days until the warts are destroyed.

Chromic acid, though a most excellent caustic, is nevertheless a dangerous one, as toxic symptoms sometimes result, and a few fatal cases are recorded. It should be applied with a camel's-hair pencil, once daily, either pure or in a 10 per cent. solution. Morrow used a solution of chromic acid, 100 grains to the ounce. White and Martin speak very commendably of caustic potash. They recommend its use in the following form:

℞.—Plumbi oxidi . . . . . 2 grains.
Potass. hydrat. . . . . 20 grains.
Aqua . . . . . q. s. ad 1 drachm.—M.

Sig.—Shake well, and apply by means of a brush to the lesion, which has previously been cleansed and dried. One or two applications are sufficient.

The silver stick or a solution of silver nitrate, 60 grains to the ounce, may be used for the same purpose; likewise pure carbolic acid or glacial acetic acid.

Treatment of Intra-urethral Papillomata. This is pre-eminently surgical. Caustic applications, however, are sometimes used; but their range of usefulness is circumscribed within pretty narrow limits, and stricture may result.

Intraurethral growths may be removed by means of the urethral forceps, the wire snare, the urethral curette, or the galvanocautery —all through the urethroscopic tube. When located anteriorly, as

is usually the case, after cocainizing the urethra they may be grasped through a meatoscope or dilating speculum by means of forceps or a silk thread. The urethroscope can then be introduced and the deeper growths removed by ligature, the incandescent snare, curette, or galvanocautery. Hemorrhage, which is usually copious and troublesome, may be controlled by direct application to the growths of adrenalin chloride solution, 1:1000. Finally, the points from which the papillomata spring should be lightly cauterized with pure carbolic acid, glacial acetic acid, or a little fused nitrate of silver upon the end of a long probe.

Treatment of Venereal Warts in Women. This is analogous to that in the male, and needs no special elaboration. In Stoner's case the warts were removed under local anæsthesia and their bases cauterized; but they persistently returned. Eventually the warts were removed and their bases cauterized under ether anæsthesia, and a permanent cure effected. Stoner says: "So extensive was the involvement of the labia that much of them had to be sacrificed with the removal of the growths. The canal (vaginal) was loosely packed with gauze and a douche of antiseptic solution was used twice daily."

Intraurethral papilloma is exceptionally rare in women. The methods of treatment are similar but simpler than in the male, owing to the comparative shortness and dilatability of the urethral canal in women.

Treatment of Anorectal Condylomata. Here, as elsewhere, absolute cleanliness is difficult, but essential. If a proctitis exists, antiseptic rectal injections (boric acid, sulphocarbolate of zinc, permanganate of potash, or nitrate of silver) should be enjoined. Dusting the warts with calomel or resorcin, or local applications of resorcin ointment, oftentimes will cure them. When rebellious to treatment they should be removed with the scissors and their bases cauterized with pure carbolic acid.

Conclusions. The following conclusions may be deduced:

1. Venereal warts, so called, are hypertrophies rather than tumors. They are inflammatory, being due to irritation.

2. These papillary overgrowths constitute from 1 to 2 per cent. of all cases of genito-urinary disease; 60 per cent. are venereal and are due to acrid, irritating discharges; the remaining 40 per cent. are non-venereal and are due to uncleanliness and maceration of their seat alone.

3. They are not confined to mankind, dogs and horses also being subject to them. Ruminants are exempt.

4. When small, the best treatment is palliative; when large, they are best removed surgically. Even then recurrences are frequent.

5. The term "papillofibroma" most correctly defines these interesting pathological new-formations.

6. The question as to whether or not venereal warts are infectious or contagious is, as yet, purely a speculative one.

7. Numerous Gram-staining bacteria are seen embedded in the epithelium and in the lymph channels. The demonstration of micrococci and bacilli in these lesions suggests that the hypertrophy and hyperplasia of tissue may be produced by certain irritating products of these bacteria.

Thanks are due Dr. John S. Fulton and Mr. John Johns for taking the photographs and photomicrographs, and Drs. A. Samuels and I. P. Robinson, both of the genito-urinary department, for invaluable aid in the compilation of statistics.

Below is attached a list of the cases referred to in the text. Only the salient features have been tabulated.

TABLE I.

Case.	Age.	Seat of growths.	Treatment.	Result.	Remarks.
1	15	Prepuce and glans penis.	Calomel and bismuth.	Cured.	Complicating gonorrhœa.
2	19	Outer surface of prepuce and coronal sulcus.	Unguentum resorcini.	Cured.	No history of venereal disease.
3	19	Coronal sulcus.	Calomel and bismuth.	Cured.	No history of venereal disease.
4	21	Sulci of frenum.	Calomel and bismuth.	Cured.	History of syphilis.
5	21	Coronal sulcus and glans penis.	Calomel and bismuth.	Cured.	No history of venereal disease.
6	21	Internal surface of prepuce.	Surgical removal.	Cured.	Complicating gonorrhœa.
7	21	Prepuce, inner and outer surface.	Surgical removal.	Cured.	Complicating gonorrhœa.
8	22	Coronal sulcus and sulci of frenum.	Unguentum resorcini.	Improved.	Herpes preputialis also present.
9	22	Coronal sulcus.	Calomel and bismuth.	Improved.	Chancroidal ulceration.
10	22	Coronal sulcus.	Unguenti resorcini.	Cured.	No venereal history.
11	25	Glans penis, coronal sulcus, and sulci of frenum.	Calomel and amylum.	Cured.	No venereal history.
12	25	Glans, coronal sulcus, and sulci of frenum.	Calomel and bismuth.	Cured.	No venereal history.
13	25	Sulci of frenum.	Calomel and bismuth.	Improved.	Chancroidal sore.
14	25	Prepuce, glans, coronal and frenal sulci.	Zinc oxide and bismuth.	Cured.	No venereal history.
15	27	Prepuce, glans, coronal and frenal sulci.	Surgical removal.	Cured.	Suppurating bubo.
16	28	Margin of anus.	Unguentum resorcini.	Cured.	Funnel-shaped rectum; proctitis.
17	32	Coronal sulcus and sulci of frenum.	Unguentum acidi salicylici.	Cured.	Had had gonorrhœa.
18	38	Margin of prepuce.	Dorsal incision; acid boracic.	Improved.	Chancre; phimosis.

TABLE II.

Case.	Age.	Seat of growths.	Treatment.	Result.	Remarks.
1	17	Back of corona glandis.	Surgical removal.	Cured	Complicating gonorrhœa.
2	19	Prepuce, corona, glans, and meatus.	Surgical removal.	Cured.	Complicating gonorrhœa.
3	22	Left sulcus of frenum.	Calomel and bismuth.	Cured.	No venereal history.
4	24	Right sulcus of frenum	Surgical removal.	Recurrence.	Complicating gonorrhœa.
5	32	Sulcus, left, of frenum.	Unguentum resorcini.	Cured.	No venereal history.

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PNEUMOCOCCUS ENDOCARDITIS.

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This subject is not a new one, for the literature upon it dates back to 1835, but it deserves attention, because there has been no extensive review of it since 1885, and since that date our knowledge has increased sufficiently to take the subject from the field of the pathologist and place it in that of the internalist. The subject to which I refer is that of acute endocarditis excited by the pneumococcus

The study of acute endocarditis has passed through the same stages of development shown by many other subjects in medicine. At first the subject attracted only limited interest from the pathologist, and only later and gradually did the subject take on clinical interest. Finally, however, it became possible to build up a sufficiently well-marked clinical picture to enable one to diagnose the condition during life in a certain percentage of the cases.

Efforts at classification of the cases were first based entirely upon the gross appearance of the exudate upon the endocardium, the verrucose and the ulcerative forms, and this classification is still maintained in various places. This is, however, a purely artificial classification, which does not correspond either to the clinical course of the cases or to the etiology.

The words benign and malignant are still frequently used in describing acute endocarditis, and, while they are not scientific, they are convenient, and, roughly speaking, correspond to the verrucose and ulcerative types.

Since the articles by Weichselbaum, in 1886, there has been no question of the fact that the ulcerative endocarditis is due to the action of a variety of bacteria, particularly the streptococci, staphylococci, pneumococci, and gonococci; but the acceptance of the idea that all cases of endocarditis, whatsoever their clinical course or the character of the endocardial exudate, are due to the action of bacteria has been less ready. There is now no reason for questioning this, the only exception to the rule being the valvular changes seen secondary to arteriosclerosis. The time has come for us to adopt an etiological classification for cases of endocarditis, although it must be admitted that demonstration of the bacteria in cases of chronic endocarditis is usually impossible, and often difficult, even in the acute cases. That the causal bacteria may be demonstrated during life in certain cases will be proved by the cases reported here.

The first case which I have to report is as follows:

Grace K., aged twenty-five years, has suffered from cardiac symptoms for about ten years. She has been well up to five weeks ago, when she began to suffer from pains in the muscles generally. The joints were free. Later, cough with mucopurulent expectoration, with dyspnœa on lying down and on exertion. No œdema. Examination shows a small, poorly nourished woman. Slight cyanosis when lying down. Rales irregularly scattered over both lungs. Apex of heart in fifth interspace beyond the nipple line. First tone palpable at apex. Presystolic thrill at apex. Second pulmonary tone accentuated and palpable. The absolute heart dulness extends to the third rib above, half an inch beyond the right border of the sternum and to the apex. Systolic and presystolic murmur at apex. Aortic tones pure. Spleen not palpable. Liver enlarged. Urine normal. Temperature, 101°; pulse, 96; respirations, 32.

Diagnosis. An acute exacerbation of an old endocarditis; mitral insufficiency and stenosis.

The temperature ranged irregularly from 99° to 105.4° for five days, and then returned to normal. Here it remained for four days, when the girl had a chill, and the temperature rose to 104°, and a pneumonia, which eventually involved the right middle and lower lobes, developed. Pericarditis developed as a complication. Pneumococci were repeatedly found in the circulating blood. The temperature fell by lysis, but the pneumococci remained in the blood for ten days after the temperature became normal.

The temperature remained normal for something over two weeks, and the patient had been out of bed for three days, when she complained of feeling poorly, and was found to have a temperature of 99° and a completely developed consolidation of the left lower lobe. The temperature ranged to 102° for two days, but the sign of consolidation persisted for several days.

Eventually the patient recovered, and left the hospital with the same lesion of heart present upon entrance.

It may be objected that the diagnosis of an acute exacerbation of an old endocarditis is not justified in this case, but I believe that the cardiac disturbance, with an irregular temperature, not accounted for by any other demonstrable process, warrants the diagnosis, and the demonstration of the pneumococci and the pneumococci only in the blood warrants the reference of the endocarditis to that organism.

Case II.—A girl, aged eighteen years, entered with the following history: Fourteen days before entrance she had a severe chill, lasting two or three hours, followed by rise of temperature, pain in the left side, and cough. After the chill, severe pain in both feet and later in knees, wrists, and elbows, lasting altogether for nearly a week. At entrance the girl had a temperature of 103.2°; pulse, 120, and respirations 42. Physical examination showed a pneumonia of both lower lobes. Painful swelling of the left hand. Heart was negative. The urine negative. Leukocytosis of 12,600. Pneumococci in the sputum. The case ran a very severe and protracted course. The maximum temperature was 106.2°, the pulse 160, and the respirations 64. It was fully expected that the girl would die, but gradually, after three weeks in the hospital—*i. e.*, at the end of the fifth week—the temperature had returned practically to normal, the pulse and respirations had slowed, and resolution was progressing. This satisfactory condition continued for five days, when the temperature began again to go up, and within twenty-four hours had reached 103.6°, with pulse of 156, and respirations of 32. Numerous joints became painful. Three days later systolic and diastolic murmurs appeared over the apex. The blood showed a moderate leukocytosis, and so many pneumococci that they could be found in every blood smear easily. Pure cultures were obtained.

The temperature remained continuously high for six days, and then returned to normal, and remained there during the long period of her convalescence. The girl left the hospital ninety-six days after entrance restored to health, but with a well-characterized double lesion of the mitral valve and orifice.

This case is striking in many ways, but particularly in that the diagnosis of pneumococcus endocarditis seems as well grounded as any clinical diagnosis can be, and yet the patient recovered. So far as I know it is the only one on record, except the case reported by Dr. Edward Wells, of Chicago, and one by Robison, of Chicago, in which cases, however, there was no demonstration of the pneumococci in the blood.

Case III.—A male, aged thirty-five years, entered about the fourth day with a pneumonia of the right lower lobe. The previous history could not be obtained, because the pulmonary condition was complicated by a serious alcoholic delirium. The temperature at entrance was 100.6°, pulse 120, and respirations 40. The heart was negative. Leukocytosis of 10,000. Pneumococci in the sputum. Urine negative. The man was seriously ill, but presented no unusual phenomenon, and the fifth day after entrance had a normal temperature, pulse, and respiration, and was apparently convalescent. This condition persisted for three and one-half days, when he had a very hard chill, and the temperature rose to 103.2°. The physical examination was negative, but three days later a systolic murmur appeared over the apex, and persisted with gradually increasing intensity to the death. The temperature ran a very irregular course, often reaching 104° or 105°, and irregularly interrupted by severe chills. The number of leukocytes fell to 6750, and although the blood was examined repeatedly for pneumococci, none were found until the thirty-second day of his illness. During the night of the thirty-first day numerous small hemorrhages appeared in the skin, particularly of the neck and thorax, but to some extent also over the limbs. Blood cultures taken the morning after the appearance of the eruptions yielded a pure culture of the pneumococci. The condition of the patient through all these days was gradually getting worse and worse, and he died during the thirty-eighth day after entrance, and the forty-second of his illness.

The clinical diagnosis was an acute endocarditis of the mitral valve, due to the pneumococcus. Fortunately, it was possible to obtain an autopsy, with the following findings: The lungs had practically returned to their normal state, although the right lower lobe, the site of the pneumonia, was somewhat firmer than the other lobe. The pleural and pericardial cavities were normal. The heart was normal in size, but showed three or four small subpericardial hemorrhages, particularly over the wall of the left ventricle. All of the valves were normal, except the mitral, which showed a polypoid, dirty, greenish-colored, irregularly granular,

firm vegetation about the size of a hazelnut. The base of this vegetation was about ½ cm. in diameter. Along the line of closure of the other portion of the mitral leaflets were small, pinhead-sized, warty vegetations. The spleen showed a single large infarct. Both kidneys were the site of infarcts, and dissection of one of the infarcts showed the embolus plugging the vessel. Smears from the vegetations taken at once showed only the pneumococci present in large numbers. The cultures, which could not be taken for some hours, were contaminated with some form of saprophytic bacilli. The cultures gave the pneumococci plus these bacilli. A rabbit inoculated through the veins of the ear with this mixture died within twenty-four hours of a lobar pneumonia, from which pure cultures of the pneumococci were obtained.

The cerebrospinal axis was not examined, but there was no reason clinically to suspect a complicating meningitis.

In 1885 Netter published a very careful and exhaustive review of this subject, covering 82 cases. Since that time 50 cases have been added, and a review of the entire 132 might be profitable.

The frequency with which pneumonia is complicated by endocarditis cannot be positively stated, because there is no reason to doubt that a certain percentage of the cases of endocarditis pass unrecognized clinically, until they later appear suffering from the effects of a chronic endocarditis. Aufrecht says that he found but a single instance of endocarditis in 1501 personal cases of pneumonia—*i. e.*, 0.06 per cent. Fismer found it twice in 230 cases—*i. e.*, 0.9 per cent. of his cases. Wells, in 6050 collected cases of pneumonia, found 19 of endocarditis—*i. e.*, 0.3 per cent., and in 1213 fatal cases there were 47 cases of endocarditis—*i. e.*, 4 per cent.

Kerr, in a review of 171 cases of pneumonia upon the autopsy table at the Cook County Hospital, found 14 instances of endocarditis—*i. e.*, 8.2 per cent. Osler reports 16 cases of endocarditis in 100 fatal pneumonias. Sears and Larrabee found 9 cases of endocarditis in 291 deaths from pneumonia—*i. e.*, 3.1 per cent. Omerod, in 183 cases of pneumonia and pleurisy, found 6 of endocarditis—*i. e.*, 3.3 per cent. Norris, in 500 cases of pneumonia from the Pennsylvania Hospital, found 5 cases of endocarditis—*i. e.*, 1 per cent. Liebermeister found endocarditis but once in 254 cases treated in the Tübingen Clinic—*i. e.*, 0.4 per cent. Sello found only 6 cases in 750—*i. e.*, 0.8 per cent. Adding these figures we get 11,243 cases of pneumonia, with 126 cases of endocarditis—a percentage of 1.1. If we take out the reports based upon the autopsy records, we find 1775 cases, with 86 instances of endocarditis—a percentage of 4.28. The percentage given by various authors ranges from the maximum of 16 per cent. in 100 fatal cases to a minimum of 0.06 per cent. by Aufrecht, from 1501 personal observations, of which 253 died; but it is probable that the average is about 1 per cent. of all cases, and 5 per cent. of the fatal cases.

What is the frequency of pneumococcus endocarditis as compared with other forms? Wells collected 517 cases of fatal endocarditis, 115, *i. e.*, 22.3 per cent., of which were in connection with pneumonia.

Lenhartz found pneumococci in 9 of 28 cases of endocarditis—*i. e.*, 32 per cent. Kerchensteiner found 6 in 23 cases of malignant endocarditis—*i. e.*, 26 per cent. Osler found pneumonic endocarditis in 25 per cent. of the cases. Kauthach and Tickell found it in 14 per cent. of 84 cases. Harbitz, in 43 cases of infectious endocarditis, found 5 due to the pneumococcus—*i. e.*, 11.6 per cent. Weichselbaum found the pneumococci in 7 of 33 cases—*i. e.*, 21.5 per cent. Totalled, these make 944 cases, with 208 associated with pneumonia—*i. e.*, 22 per cent. Taking the 127 cases of malignant endocarditis studied bacteriologically by Lenhartz, Kerchensteiner, Harbitz, and Weichselbaum, we find 27 due to the pneumococcus—*i. e.*, 21.2 per cent. Only the streptococci and staphylococci are found more often than the pneumococci in the fatal endocarditis, and they are only a little more frequent.

The relative frequency of the verrucose and ulcerative endocarditis is not to-day a matter of great importance, for we now realize that the two forms differ in degree only, and not at all in kind. In a general way, however, it is true that the greater the exudate upon the valves the greater the seriousness of the case, and while the pneumococcus may cause either small or large vegetations upon the valves, they are generally large. In some cases both large and small vegetations are found in the same case. Case II. of the personal cases reported above will serve as an illustration of this. Of 39 cases published since the article of Netter, in which the character of the endocardial exudate is mentioned, 30 are described as large, polypoid, cauliflower-like, ulcerative; 7 are described as small and warty, and in 2 cases both forms of exudate occur. Of the 14 cases in Kerr's report, 12 are described as ulcerative, and 2 as vegetative. Osler, in 16 cases, found 5 verrucose and 11 ulcerative. Norris describes 4 out of his 5 cases as malignant. These cases would place the severer forms of endocarditis at 77 per cent., the milder at 20 per cent., and both together at 3 per cent. In other words, if an endocarditis develops in the course of a pneumonia, it is four to one that it will be of the so-called ulcerative or malignant type.

The descriptions of the valvular exudate given by the various authors correspond closely. The exudate is often large, described as the size of a pea, a bean, a walnut, and up to an inch and a half in length. Cauliflower-like is a word frequently employed in the description, and is appropriate to a considerable number of the cases. The mass is firm and granular, reddish-gray, yellow to green in color. Polypoid is another word constantly recurring in the reports. Aneurysm and perforation of the valves is less com-

mon in cases due to the pneumococcus than in those due to the staphylococcus and streptococcus. Kerchensteiner regards the following features as characteristic of pneumococcus vegetations: 1. Midway between ulcerative and verrucose form. 2. Large vegetations, with wide base. 3. Smooth, discolored surface. 4. Tendency toward softening. I do not, however, place any confidence in this effort at characterization of the pneumococcus vegetations, for just as the pneumococcus may produce vegetations ranging from the smallest to the largest, so, also may any of the numerous bacteria now known to be capable of exciting endocarditis. The only way in which one can determine the bacteria exciting the endocarditis is by examination of the exudate.

While the inference always is that an endocarditis occurring with a pneumonia is due to the pneumococcus, a few exceptions have been recorded. Thus Jaccoud, in his clinical lectures of 1885 and 1886, reports a case of pneumonia complicated by endocarditis in which a streptococcus was the cause. There are reports of 69 cases, which include a bacteriological examination. In but 9 of these is there any report of the ante-mortem examination of the blood for bacteria, and 3 of these are the personal cases reported above. In 1 other case, that of Dr. Wells, the blood was examined for this purpose, but with negative results. The reason for this is that the bulk of the reports antedate the introduction of the modern methods of taking blood cultures, which are modifying our ideas on so many subjects.

In 64 cases only the pneumococcus was found—three times in connection with the streptococcus, once streptococcus only, and once streptococcus and staphylococcus. Something over 94 per cent. of the cases of endocarditis complicating pneumonia are due to the action of the pneumococcus.

There are reports covering 141 cases,[1] in which the valves affected are stated. In 116 of these the endocarditis is confined to the left side of the heart, in 17 to the right heart, and in 8 both sides are affected. Put into percentages, the figures are 82.2 per cent. left, 12 per cent. right, and 5.7 per cent. bilateral. A comparison of these percentages with those derived from the 2435 of valvular lesions tabulated by Jürgensen, in his article upon endocarditis in the Nothnagel *System*, is interesting. These percentages are 94.3 per cent. left heart, 2.7 per cent. right heart, and 2.8 per cent. bilateral.

To put it in another way: In 17.8 per cent. of the cases of pneumococcus endocarditis the right heart is affected, while only 6.7 per cent. of cases of endocarditis in general are right-sided.

[1] The number of cases, as stated earlier in the article, 132, includes only those given with clinical details. There are nine other cases, in which only the valve affected and the relation to pneumonia is stated.

The distribution among the valves is shown in the following table:

Aortic only	56	39.7 per ct.
Mitral only	40	28.3 "
Aortic and mitral	20	14.1 "
Tricuspid only	12	8.5 "
Pulmonary only	5	3.5 "
Aortic, mitral, and tricuspid	5	3.5 "
Mitral and tricuspid	2	1.4 "
Aortic and tricuspid	1	0.7 "
	141	

Comparing these percentages with those derived from Jürgensen's table, we have:

Aortic only	39.7 per ct.	18.7 per ct.
Mitral only	28.3 "	66.3 "
Aortic and mitral	14.1 "	9.2 "
Tricuspid only	8.5 "	0.4 "
Pulmonary only	3.5 "	2.3 "
Aortic, mitral, and tricuspid	3.5 "	1.0 "
Mitral and tricuspid	1.4 "	1.8 "

The striking things about this table are that the pneumococcus is something over twice as apt to involve the aortic valves as the other bacteria, and about one-third as apt to involve the mitral, while it attacks the tricuspid valve twenty times as often.

Another question bearing upon the site and character of the exudate is that of infarcts. It has been repeatedly stated that infarcts are exceptional in this class of cases, but in 20 of the 50 cases added to those of Netter infarcts were found in spleen, kidney, lungs, brain, or intestine; six in the spleen only, twice in kidney only, seven in spleen and kidney both, four times in the lungs, and twice in the brain. From this we must say that infarcts do occur with this form of endocarditis.

In 1862 Heschl drew attention by a report of 5 cases to the frequency with which endocarditis complicating pneumonia is found in association with meningitis. Netter fully confirmed this statement, for he found the coincidence of these two complications in no less than 45 of 63 cases, in which the records were sufficiently full to supply information upon this point. This amounts to 71.4 per cent. Of the 50 cases since Netter's paper, 19 had a meningitis, a rather smaller percentage, and together the percentage is 56.6 per cent.

Meningitis is a much commoner complication of pneumonia than endocarditis, and while approximately 60 per cent. of the cases of endocarditis are associated with meningitis, only about 30 per cent. of the cases of the latter are accompanied by the former.

What are the factors which favor the development of a complicating endocarditis?

Of 132 cases, 92 are males and 40 females—*i. e.*, 69 per cent. and 31 per cent.

It is generally stated that pneumonia is from three and one-half to four times as common in males as in females, and the figures quoted place endocarditis in males at approximately twice as common as in the females. It would seem, therefore, that the female is about twice as prone to endocarditis as the males.

A consideration of the age of the patients brings out some interesting facts. The following table shows the percentage of cases of endocarditis, distributed according to decades, and in comparison with them the age distribution of cases of pneumonia as derived from Aufrecht's article:

	Pneumococcus endocarditis.		Pneumonia.
1st decade	2	1.4 per ct.	6.8 per ct.
2d decade	8	5.7 "	22.2 "
3d decade	15	10.8 "	29.0 "
4th decade	42	30.4 "	17.0 "
5th decade	27	19.5 "	13.0 "
6th decade	29	21.0 "	5.5 "
7th decade and over . . .	15	10.8 "	6.0 "

This shows that while 58 per cent. of all cases of pneumonia occur during the first three decades only, 17.9 of the cases of pneumococcus endocarditis occur during the same period; that the fourth, fifth, and sixth decades supply 35.5 per cent. of the pneumonias and 70.9 per cent. of the endocarditis. This is in marked contrast to other infectious diseases, which are prone to involve the endocardium. The rheumatism, for example, causing endocarditis in a large percentage of even mild cases under twenty, while it rather infrequently involved the endocardium in the adult.

The influence of an antecedent endocarditis is considerable. Thus, of the 50 cases added in this article, 12—approximately 25 per cent.—showed old endocarditis upon which fresh vegetations had developed. Sears and Larrabee state that of the 945 cases reviewed by them, 80 had chronic endocarditis; that 4 of these went to the autopsy table, and 3 of them showed a fresh endocarditis.

Other factors which may be considered as having a predisposing influence toward the development of endocarditis are alcoholism, anæmia, debility, or malnutrition from any cause. The character of the epidemic seems to have some influence upon this, as upon other complications; for example, Netter knew of 7 cases in the various hospitals of Paris during the year 1885. Pathological specimens from 3 cases were shown before the Chicago Medical Society during the current year.

The manner in which the pneumococci become implanted upon an intact endocardium is as obscure as the reason why they prefer the aortic to the mitral valves. The experimental production of endocarditis by inoculation with the pneumococcus is usually unsuccessful, unless the valves are previously injured by the method of Orth and Wyssokowitsch, but occasionally endocarditis results without any antecedent injury. Michaelis, in 1895, showed the

heart of a dog which died in the course of immunization to the pneumococcus from an acute endocarditis of the aortic and mitral valves. The pneumococci were demonstrated in the vegetations.

It has been suggested that the endothelial cells, which possess the power of protruding pseudopodia and are also phagocytic take up the bacteria from the blood. If the bacteria are thus destroyed well and good, but if, on the other hand, the endothelial cells are destroyed the surface of the valve is roughened, fibrin cells and more bacteria are deposited, and endocarditis results.

One might infer that the pneumococci in these cases are particularly virulent, but upon this point we have very little information. Fraenkel reports a case of malignant endocarditis due to the pneumococcus lasting six months. The cocci were repeatedly obtained by blood cultures, but were of such reduced virulence that they did not cause fatal septicæmia in animals.

Turning, now, to the clinical aspect of this condition, it becomes necessary to divide the cases into two groups: those which are latent—*i. e.*, do not cause any symptoms which permit of their clinical recognition—and, secondly, those in which the clinical diagnosis is possible.

The first group is and must remain the larger. When the endocarditis develops during the height of a pneumonia the constitutional symptoms would be lost in those of the primary localization of the pneumococcus, and the physical signs from the heart require time for their development, so that death occurs before there is data upon which to base the clinical diagnosis. The possibility of an endocarditis should be kept in mind, particularly with patients beyond thirty years of age, and of the female sex. Frequently repeated and careful examinations of the heart will detect an endocarditis which must otherwise be overlooked. One must not, however, be too ready with the diagnosis. With pneumonia, as with the other infectious fevers, systolic murmurs frequently appear without there being an endocarditis. Systolic murmurs without any supporting evidence should be looked upon as accidental. Diastolic murmurs here, as elsewhere, have a high significance, and, appearing in the course of a pneumonia, must be referred to an endocarditis.

The symptoms resulting from pneumococcus endocarditis do not present any marked difference from those resulting from endocarditis from other bacteria. Temperature is present in practically every case, although in rare instances there is no temperature. Lesage and Pineau report a case of three months' duration without there being at any time any elevation of temperature. The temperature is usually very irregular, interrupted by chills, repeated at irregular intervals, and rising frequently to 104° or 105°. Exceptions sometimes occur, and show a continuous or regularly intermittent fever. The temperature of the pneumonia may pass without

interruption into that of the endocarditis, but in a very considerable proportion of the cases there is a period of a few days of freedom from fever intervening.

Netter was familiar with this afebrile period, but gives no accurate data. Of 20 cases in which there is an afebrile period, it is found to vary from a portion of one day up to twelve and more. In 4 of these cases this period is said to have been several days, without specifying the number; 13 of the other 16 had a period of seven days or less, and 10 of these 13 showed a period of four days or less.

The duration of the temperature varies over wide limits, from a few days to weeks or months. Inasmuch as it is never possible to fix the exact date of the onset of the endocarditis, the figures here given are for the entire duration of the illness. This is given in 109 of the reported cases, and ranges from a minimum of seven days to a maximum of one hundred and eighty days, and averages thirty days.

As a general proposition, those cases in which a meningitis develops are shorter than the others, but even with this complication they may last for weeks.

The pulse rate in the cases varies so greatly that it is as impossible to make any general statement in regard to it as it is in regard to the course of the temperature. The pulse rate may follow the course of the temperature, and be proportionate to it, but in other cases it is far more rapid than the temperature would lead one to expect, while in other cases there is a marked bradycardia. The bradycardia in some cases is the result of a complicating meningitis, but is also seen in cases which do not present any manifestations of the latter.

The pulse rate is greatly influenced by movement, a change in position causing an abnormal amount of change in the rate of the heart's action. There is often also marked change in the pulse count from minute to minute.

So far as subjective symptoms referable to the heart are concerned, they are the exception rather than the rule, and when they are prominent are practically always the result of an old heart lesion. Palpitation, oppression, and pain may occur.

Physical signs are entirely lacking in many of the cases. Here, as with other forms of endocarditis, the auscultatory signs appear before the percussorial. The site and time of the resultant murmur or murmurs are of course determined by the site of the endocarditis. If the murmur is purely systolic one must be cautious about its interpretation. A well-localized systolic murmur, which persists and which gradually increases in intensity, must be looked upon with anxiety, if there are constitutional symptoms not sufficiently accounted for by a process elsewhere in the body; but, again, we must urge a caution against mistaking the often loud systolic murmur, found over the hearts of people who are or have been seriously ill, for one due to actual endocardial changes.

If diastolic murmurs appear, they may be safely referred to an endocarditis.

In a certain proportion of the cases a pericarditis develops, and it may be impossible to determine clinically whether the murmurs heard are endocardial or pericardial.

Changes in the size and shape of the area of cardiac dulness are found in a certain small proportion of the cases, even in those in which the endocarditis is purely acute.

Alteration in the rate and rhythm of the respirations is due rather to the changes in the lungs and pleuræ than to those in the heart, but the possibility of pulmonary infarction must be kept in mind in the cases in which the right heart is involved. The symptoms of such infarction are determined largely by the size of the infarct, and vary from nothing at all to severe and sudden dyspnœa and hæmoptysis.

Urinary changes are those common to infectious processes; concentrated and high-colored urine, in which albumin and casts are often found. If infarcts are formed in the kidney—and this, as has been pointed out, occurs rather frequently—the kidney may become painful and blood appear in the urine. In many cases no clinical symptoms result, or are overlooked in the multitude of other and more striking features.

The spleen is often enlarged, the tumor being a part of the picture of a severe infection. It also is a frequent site of infarction, which may show itself by pain and sudden increase in the size of the spleen. A localized peritonitis often results, and may cause audible and palpable friction. The liver in some cases is swollen from passive congestion, and jaundice may occur. The exact etiology of such jaundice is as obscure here as in other severe acute infections.

A small percentage of the cases show changes in the skin in the way of localized erythema, or more often in the shape of purpura. Herpes, particularly over the distribution of the middle and lower branches of the fifth cranial nerve, is common here, as in other instances of infection with the pneumococcus.

Arthritis is a rather frequent complication of these cases, and while this has been proven to be due to the pneumococcus, in but few instances, it is highly probable that the organism could be demonstrated in the bulk of these cases.

Last, and in some ways the most important, are the blood changes. Leukocytosis is the rule in pneumococcus infections, but, exceptionally, and this is particularly true in very severe cases, among which we must place those in which endocarditis has occurred, the white blood corpuscles are often not at all increased in number; may be even reduced. The red blood cells and the hæmoglobin are reduced. More important still is the fact that the pneumococcus can be demonstrated by culture or by smear from the circulating blood. The number of cases in which this has been so far

done is still small, only 9 in number, but in view of the fact that the pneumococci are found in the blood in something over 80 per cent. of all cases of pneumonia, we must believe that they would be found equally often in this class of cases, if sought for in the proper manner. Repeated examination may be required, as is illustrated by the third of the personal cases reported, in which repeated effort failed to find them until after the appearance of the purpura, when they were very readily found.

The diagnosis of an endocarditis must rest upon physical signs, which should be faithfully looked for in all cases of pneumonia, and particularly in a case which does not end at the proper time, but runs over into a high and irregular temperature, with repeated chills. If such a temperature is not accounted for by a delayed resolution, an empyema or some other demonstrable complication, the possibility, even probability, of a complicating endocarditis must be seriously in mind, even though the physical examination of the heart shows nothing.

Before leaving this question it should be stated that the pneumococcus can excite an endocarditis without there being any involvement of the lungs at any time. In such cases the clinical diagnosis may not be carried beyond the point of diagnosing an acute endocarditis, unless the bacteriological examination of the blood shows the pneumococci.

The prognosis is shown by the fact that in the 132 cases there are but 4 recoveries, and in but 1 of these is the diagnosis complete—*i. e.*, an endocarditis is observed at the time the pneumococci are circulating in the blood. I am not, however, of the opinion that this represents the true mortality rate, for I cannot but believe that there are cases of pneumonia which recover even though there is a complicating endocarditis.

No one who has ever seen the heart from a case of this sort has much to say in regard to the treatment, for its futility is too obvious. If the vegetations are small, the virulence of the bacteria low, the resistance of the individual high, the patient may recover, but these factors cannot be estimated in the present state of our knowledge, and only the last one can be influenced.

Proper food; absolute quiet, physical and mental; stimulant medication, the reduction of temperature by hydrotherapy, and the use of the ice-bag over the heart practically exhaust our therapeutic means. Various drugs, such as the salicylates, the oil of wintergreen, the creosote derivatives, silver salts, and others are employed, but, it must be admitted, without demonstrable effects.

Conclusions. 1. Endocarditis complicates pneumonia in about 1 per cent. of all cases, and in 5 per cent. of the fatal cases.

2. Endocarditis due to the pneumococcus makes about 25 per cent. of all cases of bacterial endocarditis.

3. The pneumococcus may cause endocarditis of any degree of

intensity, but in over three-fourths of the cases it is of the severe or so-called malignant type.

4. The exudate is usually massive, but there is less disposition to ulceration and perforation of the valves than in endocarditis due to the streptococci and staphylococci.

5. The endocarditis complicating pneumonia is almost always due to the pneumococcus, although it may be due to other bacteria.

6. Pneumococcus endocarditis is much more often left than right-sided, but involvement of the tricuspid and pulmonary valves occurs about four times as often as it does with endocarditis in general.

7. The pneumococcus attacks the aortic valves more often than the mitral, and relatively twice as often as the other organisms commonly causing endocarditis.

8. The pneumococcus attacks the mitral valve relatively only half as often as other organisms, while it attacks the tricuspid about twenty times as often.

9. Infarcts occur in about one-half the cases.

10. Meningitis complicates the pneumococcus endocarditis in about 60 per cent. of the cases.

11. Pneumococcus endocarditis is relatively twice as common in females as in males.

12. Endocarditis complicates pneumonia much more frequently after thirty years of age than before.

13. An old heart lesion favors the development of pneumococcus endocarditis.

14. The clinical picture of pneumococcus endocarditis does not differ from that due to any acute endocarditis.

15. The endocarditis may develop before, during, or after the pulmonary involvement, but the pneumococci may infect the endocardium without there being at any time any involvement of the lungs.

16. A considerable number of the cases show a period of normal temperature between the fever due to the pneumonia and that due to the endocarditis.

17. This afebrile period is rarely longer than a week, and is usually only three or four days.

18. The endocarditis may be afebrile.

19. The duration varies from a few days up to months.

20. The pulse is usually rapid and irritable, but bradycardia is more frequent than in other forms of acute endocarditis.

21. Subjective symptoms referable to the heart are usually absent, except in cases where there is an old heart lesion, when they are due to the old rather than the fresh endocarditis.

22. Physical signs of the endocarditis are often entirely lacking.

23. Signs and symptoms from other organs are either those common to infectious processes or are due to infarcts, in which case they vary with the size and site of the infarct.

24. Leukocytosis is frequently absent.

25. Blood culture, carefully and perhaps frequently repeated, will show the pneumococci.

26. The diagnosis is difficult, impossible, in fact, in cases in which the endocarditis develops during the course of the pneumonia, and ends rapidly in death.

27. Endocarditis should always be suspected in a case of pneumonia which is followed by an irregular temperature not sufficiently accounted for by some other complication, such as empyema.

28. Case II. of the personal cases is the only one so far recorded ending in recovery, admitting for the sake of argument that Case I. is really not what it was supposed to be. The cases of Wells and Robison lack the demonstration of the pneumococci in the blood.

29. The prognosis is extremely grave, for 60 per cent. of the cases have a complicating meningitis, but it is probable that the percentage of recovery is higher than the reports so far published would lead one to infer.

30. The treatment consists merely in rest, absolute rest, with good, supporting food, and stimulation as required.

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A CONTRIBUTION TO THE STUDY OF ULCERATIVE ENDOCARDITIS.

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It is the writer's intention in this article to give a short *résumé* of the history of ulcerative endocarditis, the pathological anatomy of the disease, and the etiological factors, together with a short synopsis of thirty-two cases.

In the recapitulation the writer takes up the varieties of the disease, with the principal symptoms as found in his collection.

The names of Bouillard and Stenhouse Kirkes are prominent among those who first recognized that there is a form of endocarditis more malignant in its course and termination than the simple acute variety.

Virchow first showed the embolic nature of the plugs occurring in the arteries.

Winge was the first, however, to describe microbes found on the valves and in the metastatic infarcts; these he described as chains of small rods or of small round granules.

Heilberg also found organisms of a similar character in a case of endocarditis in a puerperal state; he excised particles of the valves and injected them into rabbits, but without effect. Numerous inoculation experiments followed, and Birch-Hirschfeld succeeded in

causing panophthalmitis in three rabbits by inoculation with fragments of valve deposits.

From 1885 to 1888 numerous interesting observations were published, most important of them being those of Netter, Weichselbaum, Orth, Wyssokowitsch, and Rosenbach. The investigations showed that by injecting into the external jugular vein pyogenic organisms, as streptococcus pyogenes, staphylococcus pyogenes aureus, and others, an artificial endocarditis could be produced. The experiments were more apt to be successful if the valves or arterial surfaces were injured before the introduction of the germs; the injury being caused by a sterilized stylet passed through the carotid artery into the left ventricle (Rosenbach). However, Dreschfeld has succeeded in producing the disease without previously wounding the valves. The resulting organisms were found on the valve surface and in the metastatic emboli.

Most recent investigators are of the opinion that the difference between *simple acute* and *ulcerative* endocarditis is one of degree, depending upon the virulence of the invading organisms or their toxins, or susceptibility on the part of the patient. Bacteria are found in the valves of both forms; almost *always* in the ulcerative variety, *often* in the simple form, and the same organisms are found in both. According to Weichselbaum, "acute endocarditis chiefly affects the valves, especially of the left heart, and appears to be practically always due to bacteria; the micro-organisms affect the valves either primarily or are derived from other organs. An anatomical distinction between ulcerative and verrucose forms can be drawn only according to the *destructive* character of the inflammation. The difference is entirely one of degree, dependent upon the quantity and the virulence of the bacteria. In the *ulcerative* variety the *necrotic destruction and the surrounding inflammation* is much more extensive than in the other, and leads to the formation of ulcers, erosion, miliary aneurysms, and perforation of the valves." Dawson Williams thinks that when the right heart is attacked it is by secondary infection.

Harbitz records 39 cases which he considers of the infectious type. In 6 cases the ulcerations had healed and presented outgrowths on the endocardium; at the edges of the vegetations masses of bacteria were aggregated, but cultures remained sterile. He makes two classifications pathologically—one with vegetations and excrescences on the endocardium, the other with destruction of tissue ulceration. Osler says that in 75 per cent. of cases the infectious form is engrafted upon a previous endocarditis. In his collection of 209 cases the tricuspid valve was involved alone in 19, the pulmonary in 15, aortic alone in 55, mitral alone in 17, aortic and mitral together in 41, heart walls in 33, and the right heart alone in 9.

Jackson reports 59 cases, with autopsies in 43. The mitral valve alone was affected in 15, the aortic in 9, both together in 10, and

the right heart showed lesions in 6 cases. Small abscesses of the brain and purulent meningitis were often seen, and organisms resembling cocci morphologically were frequently found in sections of the endocardium.

In 44 cases of the ulcerative type reported by Thayer and Lazear the right heart was affected in 15.91 per cent.

Out of 802 *benign* cases in the Münich statistics the right heart alone was affected in 3.25 per cent.[1]

The *organisms* most frequently found are the streptococcus pyogenes, staphylococcus pyogenes albus and aureus, pneumococcus of Fraenkel, or diplococcus lanceolatus; less frequently the gonococcus, typhoid bacillus, bacillus of tuberculosis, bacillus of diphtheria, and the colon bacillus. Streptococcus pyogenes and staphylococcus pyogenes aureus are found in cases in which the endocarditis is apparently primary; in septic and pyæmic conditions, as wounds, abscesses, the puerperal state, erysipelas, etc.; in cases where there is a pre-existing valvular lesion, due to previous rheumatic disease. These two organisms have also been found upon the valves in cases complicating typhoid fever, gonorrhœa, diphtheria, etc., as showing a type of mixed infection. The diplococcus lanceolatus has been found mostly where croupous pneumonia or meningitis has been present, although two cases are cited in this series where neither lesion existed, but a previous endocarditis had occurred.

Blood cultures were taken in 23 of Jackson's 59 cases; streptococcus was found in 8, micrococcus lanceolatus in 5, staphylococcus in 3, colon in 1, streptococcus and staphylococcus together in 1, and streptococcus with unknown organisms in 1.

Of the writer's cases staphylococcus was found in 4, micrococcus lanceolatus in 3, staphylococcus and pneumococcus together in 1, streptococcus in 2 cases.

According to Dreschfeld "the following types of malignant endocarditis are recognized: (*a*) primary; (*b*) as a complication of septic diseases; (*c*) as a complication of pneumonia and meningitis; (*d*) as a mixed infection secondary to the acute infectious fevers, to rheumatic endocarditis, or to a sclerosis of the valves."

The primary cases are admittedly rare. Pneumonia is a frequent cause, as is meningitis, also septicæmia from whatever origin; rheumatic fever, and less frequently typhoid fever, influenza, diphtheria, scarlet fever, tuberculosis, variola, and measles,.

Of the writer's 32 cases 8 occurred coincidently with rheumatism, 1 apparently with a strain of the back accompanied by hæmaturia, 7 gave a history of old rheumatic attacks, 3 of having had scarlet fever or diphtheria. 2 of palpitation and dyspnœa, 7 of typhoid

[1] In looking up the records of cases of *simple* mitral stenosis the writer has collected 50 cases, in which 12 (24 per cent.) showed lesions of the tricuspid valve. These give the largest percentage of right heart inflammation he has yet seen (report of the Cornell University Dispensary, 1904).

fever, influenza, or malaria, the remainder having apparently always been well.

The disease is rare among young children. Osler gives but 3 cases in his collection of 109. The records of the Children's Hospital at Melbourne furnish but 1 case in ten years. Davies finds but 1 case in the *Transactions of the Pathological Society* (London). Only 1 case appears in the records of the London Hospital for Sick Children from 1870 to 1890, and S. S. Adams reports but 1 case in the Children's Hospital, Washington, D. C., since 1870.

S. S. Adams has collected all the cases reported in children under fifteen years of age—46 in all—3 congenital, 1 of eight months, 1 of ten months, 1 of eleven months, 3 of three years, 2 of four years, 3 of five and a half years, 2 of six years, and the others of seven and over. The diseases preceding or accompanying this condition were: maternal erysipelas and fetal infection (cultures from the cord showed streptococci); malaria, 1 (æstivo-autumnal); acute miliary tuberculosis, 1; vaginitis, 1; remitting fever, 1; rheumatism, 3; chorea, 2; rheumatism and chorea, 1; typhoid fever, 2; empyema, 1; trauma, 1; otitis media, 1; old cardiac disease, 5; caseous tubercle, 1; diphtheria, 1; influenza, 2; erysipelas, 1; tonsillitis, 1. The rest are not given.

Of the 46 cases, the heart wall was affected in 6, the tricuspid valve in 5, the pulmonary valve in 2; one had a patent foramen ovale, and in the others the left heart was the seat of inflammation.

No cases have occurred in young children in the Presbyterian Hospital during the last ten years.

Group I.

The following collection of cases is one in which the staphylococcus pyogenes aureus was found. The albus, which was obtained in a number of cases, is considered only as a skin contamination.

Case I.—Aged thirty-seven years, male, attendant, admitted February 3, 1900; died February 9, 1900. Two of the family died of pulmonary tuberculosis. The patient drank moderately, but never had syphilis or rheumatism.

The present illness began one week before admission with the sudden vomiting of about a pint of blood, followed by a pain over both hypochondriac regions. Three days later he had retention of urine.

The *physical examination* upon admission showed nothing, but the following day the temperature began to rise irregularly, reaching 107° on the third day, continuing on the fourth day, and then falling slowly to 103°. During this time he developed a pericardial friction sound. The second day he had three convulsions, with great increase in arterial tension. Examination of the urine showed 15 per cent. of albumin (by volume), hyaline and granular casts,

and red blood cells. Symptoms of meningitis soon followed, with headache, violent delirium, retraction of the head, rigidity of the muscles of the neck, back, and extremities, and general hyperæsthesia. Blood culture proved a pure growth of staphylococcus pyogenes aureus. There were no petechial hemorrhages, no chills; there was no splenic enlargement, nor any reaction to Widal test.

Upon *autopsy* the heart weighed nine and one-half ounces; the pericardium was normal, but the mitral valve showed small, white, soft, vegetations; the spleen and the kidneys were apparently normal.

Cultures from the spleen and brain showed staphylococcus pyogenes aureus.

CASE II.—Aged twenty-five years, housewife; admitted May 7, 1899; died May 9, 1899.

There was no family or previous history of note, with the exception of an attack of rheumatism fourteen months before admission. Dating from this, however, the patient had attacks of cardiac palpitation and dyspnœa.

The present illness began five days before admission, with sudden vomiting, dizziness, and high fever, preceded by dull pain in the joints. Two days after this a bright-red eruption occurred on her feet and legs, accompanied by severe epistaxis.

The *physical examination* showed evidence of mitral insufficiency; the presence of a rather profuse hemorrhagic eruption, and marked delirium. The temperature was 106°, pulse 120. After admission the temperature continued high. The blood showed 19,000 leukocytes per c.mm. Culture gave an abundant growth of staphylococcus pyogenes aureus. There were no chills, no splenic enlargement, and no reaction to Widal test. Autopsy could not be obtained.

CASE III.—Aged eighteen years, housewife; admitted February 17, 1902; died February 21, 1902.

The patient was a premature child, and while young had scarlet fever, diphtheria, acute articular rheumatism, and typhoid fever. She had frequent attacks of cardiac palpitation and dyspnœa, and during her pregnancies was uræmic; she was not alcoholic, but was a confirmed tea drinker. For eleven weeks previous to admission she was short of breath, had dyspnœa and palpitation, nausea, occasional vomiting, and diarrhœa.

Examination revealed a dilated heart, in which evidence of mitral and tricuspid incompetency existed; there was subcutaneous œdema, and dropsy of the serous cavities. The liver and spleen were both palpable. The course of the temperature was from 103° to 104°, and continuous. The blood examination revealed 37,000 leukocytes to the cubic millimeter, and the presenee of staphylococcus pyogenes aureus; there was no reaction to Widal test. The urine contained a trace of albumin and much blood. There were no subcutaneous hemorrhages.

CASE IV.—Aged thirty-six years, male, butcher; admitted October 31, 1901; died November 14, 1901.

Family history was unimportant. The patient had rheumatism of the subacute variety at twenty-five years of age, and gonorrhœa four years ago. For four months before admission he felt languid and listless, with dyspnœa, dry cough, precordial pain; at two different periods he had profuse hemorrhagic eruptions.

Upon *physical examination* mitral, systolic, and aortic diastolic murmurs were heard; the heart was enlarged, and compensation had broken. The liver could be felt three inches below the costal margin. The spleen was enlarged. After admission petechial hemorrhages developed. The temperature was irregular and not higher than 101°, the pulse 168. Leukocytes, 27,000 per c.mm.; hæmoglobin, 85 per cent. A growth of staphylococcus pyogenes aureus was obtained upon culture. No autopsy was granted.

GROUP II.

The following cases constitute a group in which the infection is by the micrococcus lanceolatus. The first two cases were reported by Dr. Walter B. James in the *Presbyterian Hospital Report* of 1898, and are here entered through his courtesy. It is of interest to note that none of them were accompanied by pulmonary complications.

CASE V.—Aged nineteen years, German; admitted May 1, 1887; died May 28, 1887.

There was no family or previous history of note. The present trouble began three months before admission, with a mild attack of inflammatory rheumatsim. The patient was told at that time she had organic heart disease. Anæmia, dyspnœa, and cardiac palpitation were the chief complaints. Two days before admission she suddenly lost the power in her right arm and leg, with complete aphasia.

Physical examination showed mental apathy; an irregular heart with a loud mitral systolic murmur heard in the axilla and over the back. The spleen percussed large, but could not be felt. There was great hypersensitiveness of the trunk and of the extremities, especially on the right side, with paralysis of that side.

The course of the temperature curve was irregular, and ranged between 101° and 105°. The leukocytes showed an increase to 14,000 per c.mm., later falling to 10,000; there were 1,806,000 red blood cells, and 43 per cent. hæmoglobin. A culture from the blood showed micrococcus lanceolatus. Examination of the urine gave 6 per cent. of albumin (by volume), no casts. She passed from fourteen to twenty ounces during the twenty-four hours.

Upon *autopsy* the heart was found to weigh fourteen ounces; upon the mitral valve, extending to the anterior surface of the

auricle, and also into the ventricle, was a large patch of vegetation, rough and ragged, but not ulcerated; the heart muscle was mottled with pale areas. The spleen was swollen and soft, with numerous white infarctions The kidneys showed septic infarction. Of cultures taken from the spleen, liver, and kidneys, those from the first two organs showed abundant growths.

CASE VI.—Aged twenty-two years, female; book-keeper; admitted July 10, 1897; discharged August 18, 1897.

There was no family history. The patient had scarlet fever and mild rheumatism as a child. For the past two months she was anæmic and did not menstruate, although not pregnant. One month before admission mild rheumatic pains again appeared, soon followed by a sudden retinal hemorrhage. At the age of fifteen years she was told of the presence of a heart murmur.

Examination showed a pronounced thrill at the apex of the heart, with presystolic and systolic murmurs over the same area. The spleen was enlarged, urine normal.

The course of the temperature continued low and irregular, not going above 102°. The blood showed 10,000 leukocytes per c.mm. Culture gave a profuse growth of micrococcus lanceolatus; petechial hemorrhages developed with sharp pain, severe and sudden, over the region of the spleen, blindness in both eyes, and left hemiplegia, in which condition she died.

CASE VII.—Aged twenty-seven years, German, male; admitted April 1, 1903; died April 3, 1903.

For two months past the patient has been feeling weak and languid; four weeks before admission he was struck violently on the head; following this injury he felt chilly and feverish, had headache, earache, and at the time of admission he was delirious. Upon *examination* his neck was stiff and rigid, and painful upon motion; his extremities were rigid and painful also. Over the mitral area a systolic thrill and murmur were appreciable. The temperature continued high, 104°. There was no splenic tumor; there were no chills. Blood examination revealed micrococcus lanceolatus; the leukocytes were 9000 per c.mm. There was no Widal reaction.

At *autopsy* the mitral valve showed two large vegetations, a cyst on one segment and perforation of another. Under the pia and arachnoid, especially around the cerebellum, was a layer of greenish pus.

GROUP III. *A Case of Mixed Infection.*

CASE VIII.—Aged forty-four years, housewife; admitted January 18, 1902; died January 28, 1902.

The patient was a moderate alcoholic. The present illness began eight days before admission, with severe and protracted headache; three days before admission a hard, shaking chill occurred, followed by fever and sweating and increased prostration.

Physical examination showed marked conjunctivitis and rhinitis, prostration, and rigidity of the neck. The cardiac impulse was in the seventh space, and a mitral systolic murmur was evident. The spleen was enlarged. Lobar pneumonia soon developed. There were 21,000 leukocytes per c.mm. Culture from the blood showed growths of micrococcus lanceolatus and staphylococcus pyogenes aureus. Culture from the nose showed micrococcus lanceolatus, and one from the eyes showed staphylococcus. The temperature was fairly continuous from 103° to 104°, with frequent rises accompanied by chills. Upon lumbar puncture 23 c.cm. of cloudy fluid was obtained, from which smears were made, showing cocci arranged in pairs. The urine contained 4 per cent. of albumin, numerous hyaline and granular casts, and pus.

Upon *autopsy* a mass of polypoid vegetations was found on the mitral valve. The lungs contained a number of minute purulent nodules. The spleen showed numerous infarctions. A layer of pus covered the base of the brain; the ventricles contained turbid serum; the right lateral sinus and the right cavernous sinus were filled with clot. The ethmoidal and sphenoidal sinuses were eroded and filled with pus. The entire cord was bathed in creamy pus.

Group IV.

The following cases are of streptococcus origin:

Case IX.—Aged twelve years, female; admitted November 28, 1902; died December 2, 1902.

The patient had no previous illness of note. For the past four weeks she suffered from headache, pains in the back, languor, nose-bleed, irregular fever, indefinite chills, with sweating and vomiting; of late she had diarrhœa.

On *examination* the cardiac impulse was found in the anterior axillary line, and a loud systolic murmur heard over the entire left anterior chest, axilla, and back. The spleen was enlarged, urine normal, no eruption. The course of the temperature was irregular, from 101° to 105°, but there were no chills. There were 14,000 leukocytes per c.mm., and streptococcus pyogenes was found upon blood culture. No malarial organisms were found. The child became semicomatose and developed a right hemiplegia. No autopsy could be obtained.

Case X.—Aged twenty-four years, housewife; admitted August 12, 1897; died August 18, 1897.

There was a moderate alcoholic history. Eight days before admission and during her menstrual period the patient ate some indigestible food. She had pain in the abdomen, with vomiting, diarrhœa, and headache. She has vomited every day, and at one time the vomitus contained a little blood. She has had chilly sensations every day.

On *admission* there was a harsh mitral systolic murmur. Spleen not palpable. A few hemorrhagic spots were present. The temperature was enteric in character and continued at 105°. Leukocytes, 17,000 per c.mm.; no reaction to Widal test. Blood culture gave a growth of streptococcus pyogenes.

Autopsy revealed minute vegetations on aortic valve, and considerable mass of fibrin on the mitral, one cup being eroded and perforated. The heart muscle showed infarcts, as did the spleen and left kidney. The brain contained a blood clot as large as an egg in the right occipital lobe.

Group V.

The following are cases in which blood cultures failed to give results, and diagnosis rests upon pathological findings or clinical signs. Some of the cases occurred when the means of culture were not as perfect as at present, and some even before cultures came into general use.

Case XI.—Aged thirty-six years, female. Old malarial and rheumatic history; rheumatic arthritis, with chills and fever for seven weeks before admission. Splenic tumor, high remittent temperature, with chills; 10,000 leukocytes. Mitral, systolic, and presystolic and aortic diastolic murmurs present.

Upon *autopsy* one cusp of the aortic valve was hypertrophied and polypoid; there was cerebral embolism.

Case XII.—Aged forty-two years, female; history of œdema of extremities, and dyspnœa for years. Present attack of ten days' duration; temperature high and continuous; leukocytes, 27,000; no spleen, no chills, no cutaneous hemorrhages. There were mitral, systolic, and presystolic murmurs.

Autopsy showed thickening of the mitral and aortic valves, atheroma of the coronary arteries, and infarcts of the lung.

Case XIII.—Aged forty-four years, male; scarlet fever, diphtheria, malaria, and nephritis formerly; alcoholic and gonorrhœal history. Present attack of ten days' duration, with strain of the back and hæmaturia. Temperature was high, but irregular, with chills; there were petechial hemorrhages, but no spleen; leukocytes, 12,000; the urine contained a trace of albumin and a few casts. Physical examination showed a double murmur at the apex.

Autopsy revealed large vegetation on the aortic valve, and infarcts of both kidneys.

Case XIV.—Aged twenty-five years, male. Former malarial and gonorrhœal history. For six weeks before admission there was irregular fever, with chills and sweating; splenic tumor; 19,000 leukocytes; no petechiæ. There was a general systolic murmur. No autopsy.

CASE XV.—Aged twenty-nine years, female; scarlet fever as a child, with attacks of cardiac palpitation, dyspnœa, and œdema following. Temperature high and continuous; splenic tumor; cutaneous hemorrhages; leukocytes, 23,000; trace of albumin, and a few hyaline and granular casts. Systolic and presystolic mitral murmurs.

Autopsy showed mitral valve greatly stenosed; aortic valve greatly stenosed, with one cusp perforated; infarcts of the lung.

CASE XVI.—Aged forty-one years, male; old malarial history, with gonorrhœa and cystitis. Irregular fever, with chills and œdema of extremities; no spleen; no hemorrhages; urine contained 10 per cent. of albumin, hyaline, and granular casts. There was a mitral systolic murmur.

Autopsy revealed enormous vegetations on the mitral valve; infarcts of the heart, liver, and spleen.

CASE XVII.—Aged twenty-six years, male; old rheumatic history, alcoholic, with gonorrhœa. Ill three months with previous endocarditis. Temperature irregular, with splenic enlargement and cutaneous hemorrhages. Mitral, systolic, and double aortic murmurs.

On *autopsy* the mitral valve was thickened and retracted; the aortic eroded and calcareous; pericardium adherent. Infarcts of the spleen.

CASE XVIII.—Aged twenty-six years, male; rheumatic, alcoholic, gonorrhœal, and specific history. For eight days headache, diarrhœa, high, continuous temperature, splenic enlargement, and cutaneous hemorrhages. The urine contained 10 per cent. of albumin, hyaline, and granular casts. There was a mitral systolic murmur.

Autopsy revealed vegetations on both mitral and aortic valves, and infarcts of the kidney.

CASE XIX.—Aged forty-three years, female. Sudden onset, with chill, fever, diarrhœa, hemiplegia; temperature was continuously high; chill was not repeated; no splenic enlargement; no hemorrhages. Mitral systolic murmur.

Autopsy. Mitral valve thickened and retracted; infarcts of spleen and kidney.

CASE XX.—Patient was in coma when admitted; temperature 104.5°; no physical signs could be made out.

Autopsy revealed a large ulceration of the mitral valve.

CASE XXI.—Female. Former attacks of grippe and malaria. Upon admission there was swelling of the joints, fever, and coma. There were petechial hemorrhages, but no spleen; the urine showed 15 per cent. albumin, hyaline, and granular casts. No physical signs.

Autopsy showed thickening of the mitral valve and infarcts of the spleen and kidneys.

CASE XXII.—Aged twenty-eight years, male. For two weeks had rheumatic pains, dyspnœa, and slight temperature; splenic enlargement; double aortic murmurs.

Autopsy showed ulceration and vegetations on the aortic valve; infarct of the spleen.

CASE XXIII.—Aged twenty-eight years, female. Rheumatism with dyspnœa and cardiac palpitation for two months; temperature irregular; splenic tumor and hemorrhages; mitral systolic and aortic systolic murmurs.

Upon autopsy, vegetations upon the mitral valve and infarcts of the spleen and kidneys were found.

CASE XXIV.—Aged twenty-four years, female. History of scarlet fever and diphtheria. Sudden onset of muscular pain, with irregular temperature, chills, and petechial eruption; albumin, 2 per cent. Mitral systolic murmur with a diastolic at base of the heart.

Autopsy showed vegetations on pulmonary valve, with perforation. Infarcts of spleen and kidney.

CASE XXV.—Aged thirty years, female. Rheumatism starting with a chill, followed by fever and sweating; temperature continued high and irregular; splenic enlargement; 15,000 leukocytes; slight evidence of nephritis, and a mitral systolic murmur.

CASE XXVI.—Aged forty-three years, female. For three months dyspnœa and œdema from a former rheumatic attack. Temperature high and irregular; leukocytes, 11,400; cutaneous hemorrhages and mitral systolic murmur.

CASE XXVII.—Aged forty-eight years, male. Rheumatic attack of seven weeks' standing; temperature irregular, with chills, spleen, cutaneous bleeding, and 16,500 leukocytes. Albumin, 20 per cent.; large hyaline and granular casts. Mitral, systolic, and aortic diastolic murmurs.

CASE XXVIII.—Aged thirty-three years, female. Sudden joint pains with vomiting and headache. Temperature irregular; splenic enlargement; leukocytes, 17,000; mitral systolic murmur.

CASE XXIX.—Aged thirty-four years, male. Sudden onset with general pains, vomiting, chill, and sweating. Continuous fever, spleen, and petechiæ; 6000 leukocytes; mitral systolic murmur.

CASE XXX.—Aged thirty-four years, male. Two months' duration, with headache and delirium. Continuous temperature, petechial hemorrhages, and mitral systolic murmur.

CASE XXXI.—Culture gave staphylococcus pyogenes albus.

Autopsy showed vegetations of aortic valve and atheroma of the coronary arteries, infarcts of the spleen, petechial hemorrhages in all the viscera.

CASE XXXII.—Aged thirty-one years, female. Sudden illness, with diarrhœa and headache; spleen, petechial hemorrhages, low and irregular temperature; 22,000 leukocytes; staphylococcus pyogenes albus were found upon culture.

Recapitulation.

From the accompanying cases it is evident that symptomatically there are a number of types of the disease.

One of sudden onset, short duration, with high continuous temperature, headache, splenic enlargement, cutaneous hemorrhages or bleeding from the mucous membranes, together with evidence of inflammation of the endocardium; here the endocarditis is but one manifestation of a severe general infection which rapidly goes on to a fatal termination.

The second form is of much longer duration, persisting for weeks, or sometimes for months, beginning gradually with irregular fever, which often becomes remittent or even intermittent, and may be accompanied by chills and sweating, gradual loss of flesh and strength; splenic tumor, hemorrhagic eruptions, abscesses, and endocarditis. This form is distinctly septic or pyæmic in its action, and presents an entirely different picture from the former.

A third class is one in which the chief factor is meningitis. Here we see signs of intense cerebral irritation, with the addition of endocarditis, enlargement of the spleen, petechial hemorrhages, septic infarctions, and often pneumonia.

Still a fourth variety is one in which the local endocardial signs and symptoms are of chief prominence, the constitutional affection being slight, except for the evidence of poor circulation.

The foregoing varieties are recognized by most authorities under the names of typhoid, septic or pyæmic, cerebral, and cardiac types, respectively, according to the predominance of the various symptoms.

There can, however, be no certain deductions drawn as to the variety of organisms causing the different clinical forms, for the conditions simulate one another too closely.

As examples of the typhoid form there are two of staphylococcus, one of streptococcus, and one of micrococcus lanceolatus infection (Cases II., III., X. and VII.).

As examples of the septic class of long duration there are 1 of streptococcus, 2 of pneumococcus, and 2 of staphylococcus infection (Cases IX., V., VI., I., and IV., respectively).

Of 3 cases of meningitis, 1 was of staphylococcus origin, 1 of mixed staphylococcus and pneumococcus origin, and 1 was of pure pneumococcus infection.

In 2 cases of pneumococcus infection there was neither pneumonia nor meningitis present.

The *endocarditis* is a pre-existing factor in most of the cases. There are instances, however, where there is no reason to suspect that a previous inflammation of the endocardium existed. We find cases where cardiac murmurs develop during the course of the disease, in which no abnormal condition existed in the heart at the

first examination. There are also numerous cases of ulcerative endocarditis, which run their course without giving any signs which would call one's attention to the heart. These are difficult of diagnosis.

In 19 of the 32 cases, the cardiac signs found upon physical examination were verified by post-mortem findings. They were mitral, 7 cases; aortic, 3 cases; mitral and aortic together, 6 cases; pulmonary, 1 case; mitral, aortic, tricuspid, and pulmonary together, 1 case; these cases also showed affection of the heart wall in 1, adherent pericardium in 1, and sclerosis of the coronary arteries in 2.

While the greater number of murmurs represent lesions of the mitral and aortic valves, we must bear in mind that in malignant endocarditis more than in the simple form of the disease, we find evidence of endocarditis of the right heart, affecting the tricuspid and pulmonary valves.

Culture. In 24 cases from which blood was taken for culture, growths were obtained in 12. Cultures taken from the viscera of these cases which came to autopsy showed the same findings, and in no instance did the two results differ. One case showed pyogenic organisms taken from the viscera in which no blood specimen was taken. There were staphylococcus pyogenes aureus, 4; streptococcus pyogenes, 2; micrococcus lanceolatus, 3 cases; pneumococcus and streptococcus together, 1 case.

The cultures were all grown in bouillon or blood serum media. Bouillon is used exclusively now, and the best results are obtained from high dilutions.

The method of blood taking is as follows: Under strict antiseptic precautions a needle is introduced into the median basilic vein and about 10 c.c. of blood withdrawn. The needle is of fairly large calibre, and is attached to a glass tube holding 10 c.c., into which the blood runs of its own accord. The whole instrument when not in use is kept clean in a larger sterilized tube.

The culture tube is a large test tube holding about 50 c.c. of bouillon. To prevent contamination a piece of sterile gauze is placed over it, and on this a wire gauze which dips for about one inch into the test tube and is bent over the edges; over this again the cotton plug is inserted. Thus the plug can be removed without exposing the surface of the culture medium.

After the needle tube has been filled with blood 3 or 4 c.c. are expressed into the culture tube or flask—preferably the former—holding 50 c.c. of bouillon. Three such culture tubes are made.

The *temperature* may rise suddenly and remain continuously high, without remissions, until death ensues. This course of temperature is generally indicative of a severe infection of short course, and is unaccompanied by chills. It simulates closely the curve of typhoid fever, and is often the cause of mistaken diagnosis.

The temperature is frequently irregular, may be low or high, accompanied by remissions or frequently by intermissions, sometimes occurring daily, so that there is a daily rise and fall of five or six degrees. These marked remissions are often accompanied by chills and profuse sweats.

The irregular type of temperature accompanies the cases of considerable standing, although occasionally they are of but short duration.

The *blood* examination shows an increase in leukocytes in all of the cases; those of high continuous temperature being (with but one exception) over 15,000 per c.mm., and frequently 20,000, 25,000, or 30,000 per c.mm. A count of less than 15,000 per c.mm. belongs to the irregular and protracted group, although occasionally a member of this class exceeds that figure.

In Jackson's series of 59 cases he found the leukocytes regularly increased from 16,000 to 20,000 per c.mm. This increase does not hold in my series of cases, for I distinctly find in the septic varieties that the leukocytes are almost invariably below 15,000 per c.mm., and frequently below 12,000 or even 10,000 per c.mm. According to Babcock (*Diseases of the Heart*) leukocytosis is the rule; but where septicæmia exists, and there is but slight increase in the leukocytes or none at all, malignant endocarditis is to be suspected. The red blood cells and hæmoglobin show the changes of secondary anæmia.

Emboli are of frequent occurrence, but vary greatly as to the seriousness of their results. When occurring in the cerebral arteries, coronary arteries, or lungs they may be quickly fatal. They occur, however, most frequently in the spleen and kidneys. The lodging of an embolus is accompanied by sudden, sharp pain in the part affected, together with a rise of temperature and frequently a chill. Such an infarct is not infrequently followed by death of tissue and abscess, thus forming a new focus of infection. Among our nineteen autopsies there were sixteen showing emboli—one in the brain, two in the lung, one of the heart muscle, the others occurring in the spleen and the kidneys, together with one in the liver.

Hemorrhages occurred in 16 of the 32 cases enumerated here, the bleeding being mostly in small pinhead spots of the petechial variety, occurring in successive crops; in a few instances, however, larger ecchymoses were to be seen. Bleeding from the mucous membranes occurs, usually as epistaxis; less frequently we find hemorrhage from the lungs, from the kidneys, or into the brain.

In our collection there were 3 cases of hemiplegia; of these 1 was of staphylococcus origin, and 2 of pneumococcus origin.

Splenic enlargement occurred in about half of the cases cited here, with greater frequency, however, in the prolonged ones; palpation of the spleen often elicits pain from congestion or as the result of previous infarction.

Nervous Symptoms. In many cases apathy precedes delirium, which is of an active character, or is low and muttering; the active delirium occurs in cases of severe general infection of the typhoid type, while mutterings and hallucinations take place in the prolonged disease of septic type. Convulsions, coma, or death may occur at any time from embolism or hemorrhage of one of the cerebral arteries. With meningitis added, the nervous symptoms take on a more severe aspect, with cerebral irritability, convulsions, stupor, or coma; retraction of the head and neck; dilated pupils, which do not react; photophobia and strabismus; excessive hyperæsthesia; marked rigidity of the muscles of the back and extremities; opisthotonos, etc.

The pulmonary symptoms are those accompanying any severe endocarditis, and are caused by venous congestion of the lungs and insufficient oxygenation of the blood; they are evidenced by cyanosis, dyspnœa, cough, mucopurulent expectoration; moist rales may be heard in the dependent portion of the chest. With pulmonary infarct we have sharp pain, sudden dyspnœa, and hæmoptysis. In case death does not ensue, evidence of consolidation follows with, perhaps, pleuritic effusion or empyema. Where pneumonia occurs its characteristic signs are added to the above.

The *urine* generally contains a trace of albumin, with a few hyaline and granular casts; a few cases show a marked nephritis, possibly independent in origin, possibly due to the irritation of the tubules by circulating bacteria or toxins, or from infarctions; in 2 cases there was a considerable quantity of blood in the urine. Where emboli occur, with softening and abscess, pyuria results.

Concerning the use of antistreptococcus serum I have collected from the literature 24 cases; 7 have resulted in recovery, and 17 have died. In some the recovery seemed to follow the injection of the serum; in others the injection apparently did no good, or did decided harm. Beneficial results have been obtained in enough cases to warrant its receiving a more thorough trial.

Summary.

1. Malignant endocarditis is a disease of bacterial origin; it differs from single acute endocarditis in the extent of endocardial inflammation and tissue necrosis; in the fact that the right heart is more often attacked; in the more frequent embolic processes which are septic in character. Micro-organisms are found in the blood during life, in the emboli, and on the heart valves after death.

2. There is nothing in the clinical appearance distinctive of any particular variety of germ causing it.

3. Primary cases are rare, though they do exist; most cases, however, accompany rheumatism, septicæmia, the acute infectious diseases, or are engrafted upon an old endocarditis.

4. Almost all are fatal; the ones due to severe infection in a few days; the septic ones in a few weeks. The first variety have a leukocytosis of 15,000 or over, the latter usually below that number, some being very slight.

5. Emboli and hemorrhages are of frequent occurrence, and may be fatal in their results.

6. The urine usually shows evidence of nephritis; it may contain blood and pus from hemorrhage or infarct.

7. Treatment is usually unavailing, excepting the serum therapy, which is of uncertain value.

8. Infants and young children seem to be almost exempt from the disease.

The thirty-two cases cited here were published at greater length in the *Report of the Presbyterian Hospital* (New York) for 1904; they occurred in the hospital during the past ten years.

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ANGIONEUROTIC ŒDEMA.

REPORT OF TWO CASES WITH THE HISTOLOGY OF A PORTION OF THE GASTRIC MUCOSA OBTAINED BY THE STOMACH-TUBE.

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(From the Clinic of Internal Medicine, Dr. Dock.)

IN recent years considerable attention has been given to a disease which was first described accurately in 1882 by Quincke,[1] who gave to it the name "acute circumscribed œdema of the skin." Strübing,[2] an early student of this disease, proposed "angioneurotic

œdema" as a more fitting designation for the symptom-complex, basing his choice on the supposed etiology of the condition. The latter name is the one by which it is generally known at present. It is a disease characterized by transient swellings in various parts of the body, as, for example, in the skin of the extremities, of the face, in the mucous membranes of the mouth, pharynx, and larynx. Severe gastrointestinal symptoms of comparatively short duration often accompany the visible swellings or alternate with them. Heredity plays a prominent role in the etiology; the duration of the disease is variable, but usually chronic. It is not my purpose, however, to discuss the various manifestations and phases of angioneurotic œdema—a disease which, in many of its aspects, still belongs to the future for determination, but rather to call attention to the gastric features of this condition, drawing particular notice to Case II., in which it has been possible for the first time, in so far as I can determine, to make a histological examination of the gastric mucosa during an attack involving the stomach. To this end the following histories are given:

Case I.—F. B., a farmer, American, aged thirty-nine years, married, was brought to the University Hospital by Dr. Snyder, of Hanover, Michigan, on June 21, 1904. The following notes were dictated by Dr. Dock while examining the patient with the clinical staff:

The patient complains of pain in the epigastrium and swelling in different parts of the body. He describes the pain as beginning in the epigastrium and spreading sometimes around to the right side, but never into the shoulder-blade or shoulder or downward. He has had these pains as long as he can remember; they come on without cause, and are accompanied by nausea and vomiting. He has them about once a month, at times as often as once a week; they have been somewhat more frequent this year than formerly. The pains last four to five hours. Morphine alone relieves them. By the next morning he is always ready to go to work.

As long as the patient can remember he has also had attacks of swelling in the hands and feet, rarely in the face, but he has had the eyes swollen shut, *e. g.*, one week ago, when the upper lip was also swollen so that it was about one inch thick. He has also had swelling of the larynx so that he can hardly speak; sometimes he feels swelling without pain in the epigastrium; sometimes feeling of "clogging" under the sternum. At times the penis swells. The tongue is never swollen. About twenty years ago he had hæmaturia; he does not remember what the blood looked like, but thinks it was present in the urine about one week. He thinks he has passed no blood since then, but the urine is "usually red." Two or three times this year he has passed blood in the stools. The general health of the patient has not been affected. Weight and strength show no change.

Status Præsens. Patient has a large frame, moderate panniculus; muscles large, but rather soft. Skin over body of natural color. Face, neck, and ears very red. Nose, cheeks, and chin show many enlarged venules. Slight rosacea of nose. Over right hand and wrist skin shows large pigmented areas, with red between, but no swelling. The left hand and forearm are swollen and the skin is red; there is a slightly elevated red patch on the front of the forearm, from the upper one-third and from the inner side to the line of the radial artery. The ball of the thumb is considerably swollen, feeling thicker and tenser than the right thumb and showing the marking of the epidermis more plainly. Palmar surface of left thumb is tense, red, and cyanotic. On back of hand moderate swelling, but not very much redder than right hand. Patient says there is itching when the swelling begins; otherwise feels nothing abnormal but a sense of tightness. Color of hands not much affected by a change of position.

Thorax is well formed; upper part of sternum and costal cartilages rather prominent; lower part of sternum slightly depressed. Epigastric angle very wide. Apex beat not distinctly seen, but there is a pulsation in the fourth intercostal space one inch inside the nipple. Heart dulness begins on the fifth rib, extends from left parasternal to left sternal line. Auscultation: heart sounds moderately strong and clear. Radial pulse: artery easily felt, is not tortuous, no irregular thickening; pulse rather small, regular, tension low.

Abdomen is on a level with the ribs in the middle, sloping slightly on the sides. The abdominal wall is rather firm, but without local rigidity. Patient does not complain of deep pressure in epigastrium or gall-bladder region, where palpation and percussion are negative. No tenderness in the back.

The patient has had trouble with his teeth for a long time. Many of them are missing; those present are mostly carious. Gums are rather spongy, with some ulceration, especially in the lower jaw.

The diagnosis of angioneurotic œdema was made, and the patient was advised to remain under the care of his home physician, and to take four minims a day of a 1 per cent. solution of nitroglycerin.

Case II.—G. W. S., a stenographer, American, aged twenty-one years, single, entered the medical clinic of the University Hospital on October 23, 1903, complaining of swellings of the hands, legs, and larynx, and of "stomach trouble."

Family History. The patient's father is living and in good health. His mother is living, but has swelling of her hands similar to that of the patient; she also has stomach trouble. The patient has two brothers living and well. His mother gave birth to one stillborn son. One sister is living; any blow on her face will cause it to swell. Another sister died at the age of eighteen months of "epilepsy." Maternal grandmother living and in good health at the age of

eighty-three years. Maternal grandfather died of unknown cause. Nothing was known of the paternal grandparents. No history of importance in other relatives was obtained.

Personal History. The patient had "mumps" at the age of twelve years. Later he had "measles" and "chicken-pox." Good recovery in each instance. When seventeen years old he had "scarlet fever," complicated with "nephritis;" since then he has been well, with the exception of the present disease.

History of the Present Disease. The patient first noticed a swelling in the hands when he was twelve years old. He thought it was due to "overheating his blood." The swelling did not last long, and the patient could not tell when it was coming on; it usually disappeared within forty-eight hours. Sometimes it came on after exertion; at other times the same amount of work caused no swelling. Later swellings appeared in his feet, then in his knees and elbows. Patient says the swelling seems to be more in the joint than in the muscles. Riding a bicycle has caused swelling of the scrotum and then of the penis. The symptoms gradually became worse. Since the attack of scarlet fever the patient's throat has troubled him, his voice being husky at times. Four years ago the patient had "œdema of the glottis," and tracheotomy was performed. He was unconscious at this time. He was confined to his bed for three weeks after the operation, during which time he says his temperature once reached 106°. While in bed the skin on the palms peeled off. It was at this time that his doctor told him he had had scarlet fever; the urine became black, and the specific gravity was 1.008, according to the patient. It was about two months before the tracheotomy wound healed; previous to the healing there was a discharge from the wound with a "fierce" odor. His throat at this time was so sore that he could eat no solid food. After recovering from this illness the patient was in fairly good condition, except for occasional swellings, until April, 1903, when he had another attack of œdema of the glottis. This came on in the morning. At noon he was unable to eat his dinner, and at 6 P.M. of the same day he was unconscious, and a second tracheotomy was performed. On July 13, 1903, the patient noticed a swelling "under the shoulder-blade" on rising in the morning. He says this gradually worked up his back, and he noticed swelling in his throat about 4 P.M. of the 13th. At this time he used a gargle containing carbolic acid. After eating supper he gradually became worse until midnight, when intubation was tried. This failed, and a trocar was thrust into the trachea. He was in bed five days at this time. About the middle of August, 1903, he again had symptoms of œdema of the glottis, which subsided with steaming. At times coincident with the swelling in the skin the patient suffers from nausea, vomiting, and sharp pain in the epigastrium, lasting one to two days. He can assign no definite cause for these attacks.

The patient is obliged to do light work, avoiding much exercise, because of the liability to produce swelling. He takes his meals regularly. Appetite is good. Does not use tobacco. Uses alcohol very moderately. He drinks tea and coffee with his meals.

On admission to the hospital at 8.30 P.M. on October 23d, Dr. Alexander noted a puffiness all over the right hand and foot, especially well marked on the palmar surface of the thumb. No œdema in left hand or foot. A few slightly raised red patches over thorax, more numerous over sternum. Irregular, red, slightly raised patches over abdomen. Skin over the rest of the body of good color, elastic, slightly moist. Temperature, 97°; respirations, 24; pulse, 72.

October 24, 1903. Laryngoscopic examination by Dr. Dock. Larynx is small; epiglottis straight, but curled from side to side. Interarytenoid space deep. Entire mucous membrane red and slightly swollen. False vocal cords project inward, almost covering the true cords in phonation. Cords slightly red. Trachea small, moderately congested. Blood pressure (Riva Rocci) 138 mm. Hg. Nitroglycerin gtt. j of a 1 per cent. solution, ordered every three hours. After two doses (7 P.M.), pressure (Riva Rocci) 134 to 137 mm. Hg. Blood examination shows 4,560,000 red cells, 10,186 whites, and 100 per cent. of hæmoglobin.

25*th*. *Status Præsens:* Temperature, 98°; respirations, 20; pulse, 76, regular, moderate rise, good tension. Systolic pressure with Cook's modification of the Riva Rocci apparatus, 125 mm. Hg. at 10 A.M. Patient is in active dorsal position; mind is clear, expression natural. Usual weight, 145 pounds. Before second tracheotomy (April, 1903) weighed 160 pounds. Present weight, 146 pounds, stripped. Height, 5 feet 11¾ inches. Patient is well built, frame fairly strong. Panniculus small. Muscles fairly developed and firm. Below the right angle of the jaw is a body about one and one-half inches long, of the thickness of a lead-pencil, which runs from below upward and backward; surface slightly uneven, no pulsation in it. Lymph glands negative. Slight swelling on dorsum of left hand over the carpal and bases of the metacarpal bones. Skin not red or shiny here. Same condition on sole of left foot, especially over the base of the great toe. Right hand and foot negative to-day. Joints otherwise negative. Skin shows slight flush over thorax. Acne eruption of moderate extent over shoulders. The rest of the skin is of good color; moist.

Pupils equal, react well. Sclerotics clear. Conjunctivæ of good color. Lips show trace of cyanosis. Teeth are in good condition. Tongue is moist, not swollen; has very thin, white coat. Voice is husky; can scarcely speak above a whisper.

Neck shows a scar about 3 cm. long, the width varying from ¼ to 1¼ cm. It is situated in the middle line just below the thyroid cartilage; skin pinkish over it. On swallowing the lower half of the

scar moves upward, being attached to the structures beneath. Right lobe of thyroid gland palpable; left not palpable.

Thorax well formed. Expansion good and symmetrical. Percussion note slightly higher pitched and less resonant over upper left front; otherwise negative. Auscultation gives slightly increased vesicular over left apex anteriorly; with this exception normal vesicular throughout. Auscultation of spoken voice negative.

Heart: Apex just visible and palpable in fourth intercostal space in the nipple line. Dulness slightly increased to the left. Both sounds heard well at apex; the first is followed by a very faint, soft, blowing murmur, which is not transmitted into the left axilla, but is heard in the third intercostal space at the left edge of the sternum. The second sound at the apex is clear. Pulmonic area: sounds clear, no accentuation. The first aortic sound is replaced by a very faint blowing murmur, which is not heard under the sternum. First sound at tricuspid area roughened.

Abdomen is just below the level of the ribs and is symmetrical. Walls moderately tense. Spleen and liver not palpable. No tenderness.

Toward the end of the examination the skin of the thorax showed a mottled erythema.

Examination of stool: large, brown, consistency of thick soup, some foam; odor foul; small amount of mucus; a few leukocytes; no red blood cells.

Urine: Day sample (7 A.M. to 7 P.M.) amounted to 800 c.c.; specific gravity 1.013; reaction neutral; slightly turbid; sediment was small in amount and contained a few polynuclear neutrophiles. Night sample (7 P.M. to 7 A.M.), 120 c.c.; specific gravity 1.030; neutral, pale yellow, moderately turbid; sediment large in amount, and contained many leukocytes and a few cylindroids. In both samples tests for sugar were negative; a trace of albumin was found in the night sample; no casts; no erythrocytes.

26th. Urine presented similar macroscopic and microscopic appearances. A differential count of the white cells of the blood showed the following percentages:

Lymphocytes	22.09 per cent.
Mononuclears	8.48 "
Transitionals	2.95 "
Polynuclear neutrophiles	64.01 "
Polynuclear eosinophiles	2.36 "

At 7.30 P.M. several fresh drops of blood were examined for filaria, no parasites being found.

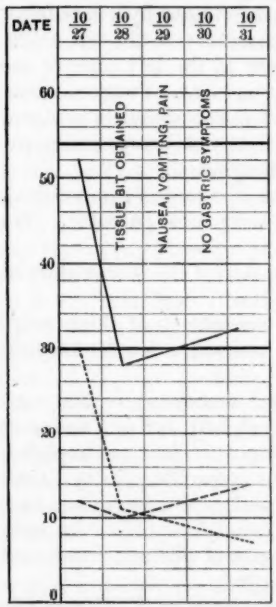
27th. Patient given an Ewald test breakfast. It remained in the stomach one hour, at the end of which time 100 c.c. were obtained. Had normal stomach odor. Contained an excess of mucus. Peptic digestion 8.5 (Mett) in ten hours. The fluid, examined chemically, showed free HCl, 30; loosely combined HCl, 12; total acidity, 52.

The microscope showed a moderately large number of leukocytes. The swelling of the left hand and foot has largely disappeared to-day.

The urine of October 27th and 28th continued to show leukocytes; otherwise it was negative.

28*th*. The patient complains of severe pain at the end of penis on micturition. This has been bothering him for the last few days, and is worse to-day. Ewald breakfast given. Remained in stomach one hour and five minutes; 130 c.c. were obtained. Lavage showed blood and a large piece of tissue. Odor normal. Free HCl, 11; loosely combined HCl, 10; total acidity, 28. No lactic acid; peptic digestion 2.2 mm. in nine and one-half hours. Microscopic examination revealed a few yeast cells.

FIG. 1.



The acidity of the gastric contents represented in cubic centimetres of $\frac{N}{10}$ NaOH.

Dotted line: free HCl.
Broken line: loosely combined HCl.
Continuous line: total acidity.

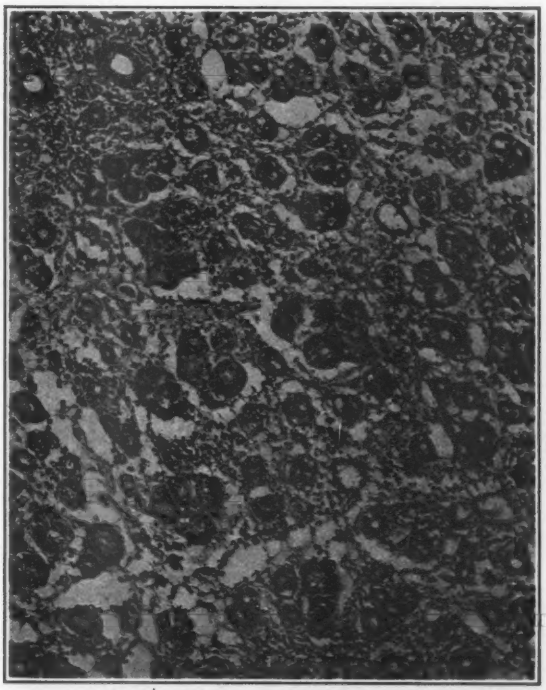
29*th*. Patient did not sleep well. At 7 A.M. felt sick at his stomach, and refused Ewald test breakfast. During the forenoon and early afternoon the patient vomited a light-greenish fluid several times, and complained of pain in his stomach. At 3 P.M. the stomach-tube was passed and the organ was washed. The patient did not vomit again until 8 P.M., having slept about an hour previous to this time. At 11 P.M. the patient was extremely nauseated and vomited considerably. Says he often has these attacks, lasting one to two days. Retching and vomiting continued, and at 1 A.M. on October 30th the stomach was washed again. Washings showed an excess of mucus; no solid particles.

The leukocytes in the urine now became about equally numerous in day and night samples. The microscopic examination showed a good many red blood cells in a mass resembling a small clot, only a few cells being scattered through the field, and a moderate number of leukocytes. In a preparation stained with methylene blue a few polynuclears and many small, round, epithelial cells with centrally placed nucleus, both singly and in patches. Many cellular casts; the latter were still present on the following day. Albumin about 1:30 by volume.

30*th*. Patient feels better to-day. Nausea, vomiting, and pain in epigastrium have ceased.

31*st*. The patient received a third Ewald breakfast to-day. This remained in the stomach one hour and five minutes; amount, 100 c.c. Chemical examination, quantitative, showed free HCl, 6; total acidity, 32.

FIG. 2.



Portion of gastric mucosa removed by stomach-tube from Case II. of angioneurotic œdema. Extreme œdema of stroma.

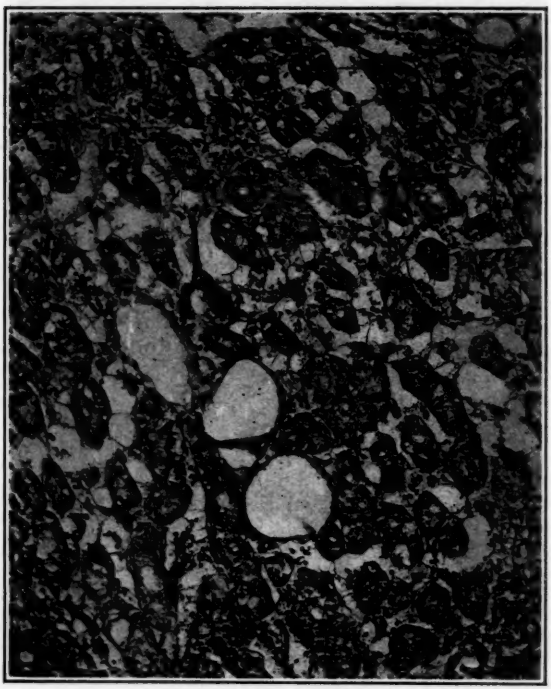
The condition of the patient remained unchanged up to November 2, 1903, when he left the hospital.

The piece of tissue which was obtained in the stomach washings from Case II. on October 28th was placed immediately in absolute alcohol and sent to the pathological laboratory for examination. The report which Dr. Warthin has made follows:

Tissue received from Dr. Dock's clinic with following description: "Semitranslucent, almost jelly-like bit of tissue obtained from

stomach washing of patient S. Put at once into strong alcohol." The tissue was examined by me in alcohol as soon as received. The bit measured 13 mm. in greatest length, 7 mm. in greatest breadth, and 4 mm. in greatest thickness. It was soft, white, smooth on one surface and slightly rough and ragged on the other, suggesting a portion of the mucous membrane. The size of the

FIG. 3.

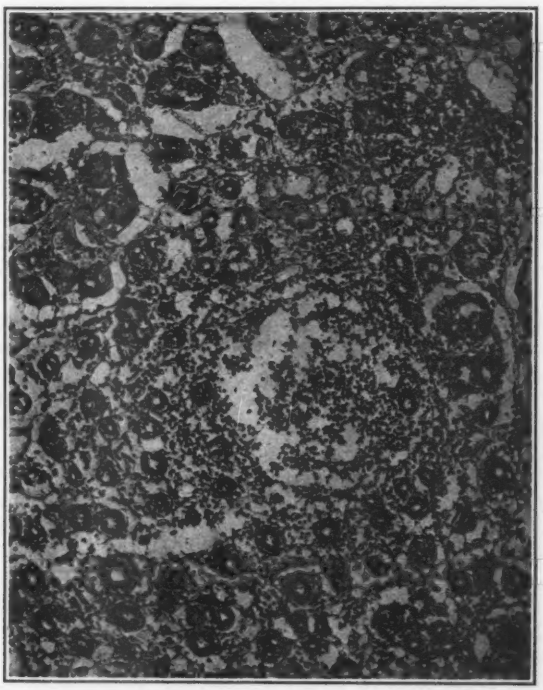


Portion of gastric mucosa removed by stomach-tube from Case II. of angioneurotic œdema. Extreme œdema. Great dilatation of lymph spaces and vessels.

bit was, however, taken as an argument against its being a portion of the gastric mucosa, as of the many bits obtained from stomach washings examined in the laboratory none had ever approached this in size. The tissue was embedded in paraffin and stained in hæmatoxylin and eosin, Van Gieson's, and kresyl-echt-violett. Microscopic examination showed, however, that the piece was gastric mucosa, most probably from the pyloric end, as few parietal cells were found in the glands and as numerous lymph nodes were

present, the character of the sections corresponding in general to that of glands from the pyloric end of the human stomach. The entire tissue presented the picture of an extreme œdema of the interstitial tissue, the lymph spaces and vessels being enormously dilated, the cells of the stroma being separated by wide spaces or vacuoles and the supporting fibres in many places separated into their ultimate fibrillæ. The glands as a rule were somewhat loosened

FIG. 4.

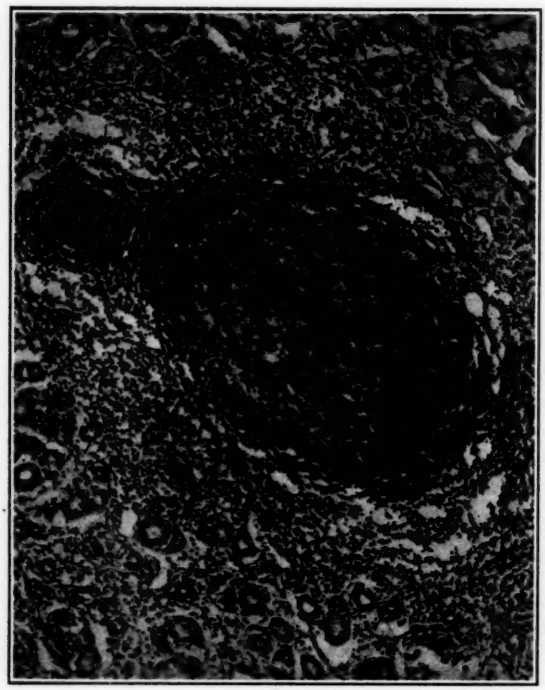


Portion of gastric mucosa removed by stomach-tube from Case II. of angioneurotic œdema. Small lymph follicle, showing marked œdema.

or contracted from their basement membranes and vacuoles were found in some of the epithelial cells. No excess of mucous formation. The œdema, however, was chiefly confined to the interstitial tissue, hence the suspicion of the tissue having been water-soaked, which was entertained at first sight, was not supported. The appearance of the vacuoles in the stroma and the dilation of the lymphatics gave, moreover, the impression of a fluid confined under pressure. A very finely granular precipitate staining red with eosin in the

lymphatics and about the edges of the vacuoles was taken as evidence of the slight albumin content of the fluid. Numerous small round cells were present in many areas, to a greater extent than is usually found in normal gastric mucosa. Many of the stroma cells contained vacuoles and were spherical and swollen. The smaller lymph nodes showed likewise an extreme œdema, the cells being widely separated. In the larger lymph follicles the œdema was

FIG. 5.



Portion of gastric mucosa removed by stomach-tube from Case II. of angioneurotic œdema. Large lymph node, showing œdema of the peripheral and central portions.

most marked about the periphery of the node and in the central portion, the cells in these places being widely separated. From all the appearances a diagnosis was given of "extreme œdema of gastric mucosa, non-inflammatory in origin."

As we see from this report, the possibility of the tissue being water-soaked was considered. This is excluded, however, not only by the practical limitation of the œdema to the interstitial tissue, but also by the fact already mentioned, namely, that the tissue was

placed in absolute alcohol as soon as it was removed from the stomach. Incarceration of the mucosa within the end of the stomach-tube is another possibility which it is necessary to keep in mind, but which can be dismissed in the present instance, as the removal of the test meal with the subsequent lavage was performed by an experienced operator. As the piece of tissue was undoubtedly obtained from a wound inflicted by the end of the tube at the time when the stomach was being washed, the conclusion is forced upon one that there was an acute, non-inflammatory œdema of the gastric mucosa.

Œdema has been looked upon from the first as the probable cause of the gastric symptoms so frequently associated with angioneurotic œdema. Quincke,[1] reasoning from analogy, looked upon the nausea, vomiting, and pain as manifestations of local œdema of the stomach. He says, "Auch auf Magen- und Darmschleimhaut dürften, nach den in einem Falle anfallsweise auftretenden gastrischen und intestinalen Symptomen zu schliessen, solche umschriebenen Schwellungen vorkommen." It is possible, also, that the periodic vomiting described by von Leyden[3] is to be attributed to œdematous swellings of the wall of the stomach. Attacks of colic of obscure origin have recently been shown by Osler,[4,5] to be manifestations of the erythema group of skin diseases, in which angioneurotic œdema is included. Strübing[2] considered the gastrointestinal symptoms the result, in part, of a local œdema, though unwilling to admit that œdema may explain all the symptoms on the part of the digestive tract; nor is it possible to disprove his view. Osler[6] was among the early writers upon the subject to indicate the probability of the stomach and intestinal symptoms being due to a local œdema; a view which he has recently reaffirmed. Fox[7] says: "It is generally conceded that the bronchial mucous membrane may be involved and a true asthma result, coinciding or alternating with outbursts of cutaneous urticaria. The implication of the digestive tube is less certain; but many authors, such as Guéneau de Mussy, accept the doctrine and thus explain certain intestinal attacks characterized by pains, diarrhœa (sanguinolent or not), melæna, or tympanites. Drs. J. J. Pringle and Hillier Chittenden have recorded cases of hæmatemesis suspected to own a similar cause, and Dr. Galloway has observed a wheal in a rabbit's stomach." Many other instances in the literature might be cited in which the nature of the gastrointestinal disturbances in angioneurotic œdema was similarly surmised.

The fall in free hydrochloric acid and in the total acidity coincident with the development of the stomach symptoms in Case II. may have been due to œdema of the mucosa. It is possible that the pain may also be explained by a stretching or pressing of the nerves or nerve endings.

As far as I have been able to determine from a careful review

of the literature, this is the first case of angioneurotic œdema in which it has been demonstrated that an œdema existed in the mucous membrane of the stomach synchronously with an attack of nausea, vomiting, and pain. Galloway's finding in the stomach of a rabbit is the only comparable instance which I have met with. My efforts to consult his original article have been unsuccessful. To conclude that all attacks of gastric disturbance met with in acute circumscribed œdema are attributable to local œdema of the stomach wall would be unwarrantable. To assume that a simple, non-inflammatory œdema is the only pathologico-anatomical alteration which may occur in the stomach in this disease would be equally unjustifiable. We can state positively, however, that simple œdema of the stomach wall does occur concomitantly with attacks of nausea, vomiting, and epigastric pain at times, at any rate, and that the probability of local œdema lying at the base of practically all of the gastrointestinal symptoms in angioneurotic œdema is greatly strengthened by this report.

It is with pleasure that I acknowledge my indebtedness to Dr. Warthin for the time and labor which he devoted to the preparation of the accompanying photomicrographs.

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PRIMARY CARCINOMA OF THE DUODENUM.

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TEXT-BOOKS, systems on internal medicine with few exceptions, and even monographs on diseases of the intestines, are singularly silent or give very little attention to malignant neoplasms of the duodenum. Indeed, such tumors occur in that part of the intestine

very rarely, but sufficiently often to give occasion for study. It is a suggestive, yet noteworthy fact, that malignant disease for the most part spares the small intestine, and, on the other hand, revels in its attacks on the stomach and the large intestine. The pylorus and the ileocæcal valve mark the limits between which tumors of a malignant nature are rarely seen, while, on the other hand, the structures forming these limits are more or less frequently involved; that is, the pylorus and the ileocæcal valve (the latter especially on its colonic surface) themselves are not infrequently the seats of a carcinoma. Cuneo and Lucène,[1] who have done much anatomical work on the lymphatics of the stomach, analyzed ten specimens of pyloric carcinoma, and in all but one found the pyloric valve the limit of invasion and growth; in only one of these specimens did the carcinoma extend from the pylorus into the duodenum. Similarly at the other end of the small intestine, while the colon is relatively not infrequently the seat of carcinoma, the ileocæcal valve forms almost a barrier to the extension of carcinoma into the ileum. When primary malignant disease does attack the duodenum or the ileum it starts from those portions of the gut much more frequently than it extends from the pylorus or the cæcum.

Frequency of Primary Malignant Disease of the Small Intestine. In Guy's Hospital between 1826 and 1893 there are records of 17,652 autopsies. Perry and Shaw[2] investigated these, and report ten cases of malignant disease of the duodenum; of these ten cases, four were carcinoma, six were sarcoma.

Fenwick[3] states that in searching the records of the London Hospital's autopsies, amounting to 19,518, the duodenum was found to be the seat of malignant growth in 18 cases.

Leichtenstern[4] gives some statistics concerning the relative frequency of carcinoma which will illustrate the relations between carcinoma of the various divisions of the intestinal tract. He says that between the years 1858 and 1870 there were 34,523 deaths at the Vienna General Hospital, of which 1874 were from cancer of different kinds. He examined the records of 4567 cases of cancer at the same hospital, and found 143 were of the rectum and 35 of the rest of the intestinal tract. Omitting cases of cancer of the rectum, he collected from published cases, records of pathological institutes and hospitals, 154 cases of intestinal carcinoma, 33 of which were of the small intestine, comprising 17 of the duodenum and jejunum and 16 of the ileum. He states that the small intestine furnishes 4.3 per cent. of the cases of cancer of the intestines in general. Utilizing his calculation and including his 616 cases of rectal cancer, we find that in 770 cases of intestinal carcinoma there were 33 of the small intestines.

From the years 1870 to 1881 inclusive, 20,480 autopsies were made at the Pathological Institute of the Vienna General Hospital, of which Maydl[5] reports 1460 were cases of cancer. Of these, 100

were cases of intestinal growths, in which the duodenum was involved only in 2 cases, the jejunum in no case, and ileum in 4 cases.

Nothnagel[6] adds to Maydl's statistics, and reports that at the same hospital between 1881 and 1893 inclusive, there were 21,358 autopsies, of which 2125 were on cases of carcinomatous growths. Of these, occurring somewhere in the entire intestinal tract, were 243, of which 5 occurred in the duodenum, none in the jejunum, and 6 in the ileum.

A. Zemann[7] from a collection of 21,624 autopsies, reports 165 intestinal carcinomata, 9 cases involving the small intestine, of which 3 involved the duodenum, none the jejunum, and 6 the ileum. These statistics come from the source from whence Nothnagel derived his.

Bryant[8] collected the reports of 110 autopsies of cases of carcinoma of the intestinal tract, of which 6 involved the small intestine. Of these I have been unable to find out how many were of the duodenum.

Müller,[9] examining the records of 5621 autopsies conducted at the Pathological Institute in Berne between the years 1886 and 1891, found 521 cases of carcinoma, of which 41 were intestinal; of these, 9 occurred in the small intestine, that is, 6 occurred in the duodenum, and 3 in the other parts of the small intestine, probably in the ileum, a relatively larger number than in the Vienna statistics.

Georg Heimann's[10] statistics, which are very exact and reliable, show that during the years 1895 and 1896 there died in the general hospitals of Prussia 20,054 patients with cancer, of whom 1706 had some part of the intestinal tract involved; of these, only 20 were of the small intestine, the number attacking the duodenum not being specifically mentioned. The last statistics are perhaps the most accurate and voluminous of any cancer statistics yet collected.

Lubarsch[11] examining the records of autopsies on deaths from carcinoma in the Pathological Institute of the Hospital of Breslau, reports 569 cases of carcinoma, among which 38 were in the large intestine, 2 in the duodenum, and 2 in the ileum.

Computing from the number of carcinomata of all organs collated by Maydl,[5] Nothnagel,[6] Müller,[9] G. Heimann,[10] and Lubarsch,[11] which amounted to 24,160 cases, we find that the general intestinal tract was involved 2128 times, 50 of these being due to carcinoma of the small intestine; in other words, carcinoma of the small intestine occurs in 2.3 per cent. of the cases of carcinoma of the intestinal canal, a figure much smaller than Leichtenstern's[4] statement of 4.3 per cent.

Or, even when using the statistics from all the previously mentioned sources, including Leichtenstern's[4] 794 intestinal cancers, but omitting A. Ziemann's,[7] whose cases were collected from the same source as Nothnagel's,[6] and adding Bryant's,[9] 110 intestinal carcinomata, we find that of 3563 cases of intestinal cancer 89 cases

involved the small intestine, or 2.5 per cent. of the whole. In either case the figure is lower than Leichtenstern's,[4] and still lower than Leube's[12] estimate, who says that carcinoma of the small intestine furnishes about 5 per cent. of all intestinal carcinoma.

We find among these cases an entire absence of specific statements of carcinoma of the jejunum.

Too much importance, further, should not be placed on deductions from statistics in determining the relative frequency of duodenal and ileal carcinoma, because there is some doubt as to the category under which carcinomata of the ileum have been placed. The most of the cases of carcinoma of the ileum occur in the region of or involve the ileocæcal valve, and on that account are classified by some as malignant disease of the small intestine, by others as of the large intestine.

In determining the frequency of carcinoma in the anatomical divisions of the small intestines we may use of the foregoing statistics only those of Maydl,[5] Nothnagel,[6] Müller,[9] and Lubarsch,[11] as the others do not specifically mention the occurrences of carcinoma in each division of the small intestine. Making this computation, we find of 4675 carcinomata, 15 occurred in the duodenum, or 0.3 per cent. of all intestinal cases, and 15 occurred in the ileum, or likewise 0.3 per cent. of the whole.

Rolleston[13] makes the statement that "the larger number of the recorded cases of malignant disease of the small intestine is found to start in the duodenum and, according to some statistics, three-quarters of the cases of malignant disease of the small intestine occur in the duodenum." This is hardly borne out by an analysis of the recorded cases and statistics. While it is true that sarcomata have their seat of preference in the small intestines, it is also true that primary sarcoma of the small intestine is much rarer than primary carcinoma of that portion of the digestive tract. Thus, Müller reports only 1 case of intestinal involvement in 102 cases of sarcoma and 41 primary intestinal carcinoma out of 521 cases of carcinoma. Nothnagel[6] in a like manner says that of 274 cases of sarcoma, 3 occurred in the intestine, and among 61 lymphosarcomata, 9 occurred in the intestine. Of the three sarcomata reported by Nothnagel, 1 occurred in the ileum, 1 in the cæcum, and 1 in the rectum; and of his 9 lymphosarcomata, 1 involved the duodenum, 3 the jejunum, 3 the ileum, and 2 the cæcum. Libman,[14] it is true, collected 15 cases of sarcoma of the duodenum, yet his cases cover most all the sarcoma of the intestines reported in which the location is stated—41 in all.

Our review of statistics does not conform with the statements of Rolleston and of many of the various authors of monographs on intestinal diseases who claim that carcinoma of the duodenum is decidedly more frequent than carcinoma of the ileum. Even such a pathologist of most extensive experience as Birch-Hirschfeld, in

the first edition of his renowned *Lehrbuch der Pathologische Anatomie,* made the same statement, but changed it in the third edition to represent the state of facts nearer the truth, by reversing his original statement and thus giving the ileum the site of greater preference for carcinomatous attack over the duodenum.

From the consideration of these statistics a fair statement would indicate that carcinoma of the duodenum occurs not more frequently than carcinoma of the ileum, that the one is as infrequent as the other, and that both are rare; that carcinoma of the jejunum is practically unknown.

The Division of the Duodenum Most Affected. In considering the topics connected with the specific observations as to the situation of the carcinoma in the duodenum, as to the variety of carcinoma, and so on, most of the later writers on duodenal carcinoma have made use of the valuable series of cases collected and reported by Whittier[15] and Pic.[16] Whittier,[15] in 1889, gathered 13 cases which had not previously been connected with any published article on the subject of duodenal carcinoma, and Pic, in 1895, 10, but of Pic's cases 2 were previously included in Whittier's series. In these two collections 21 cases are, therefore, distinct. The great trouble with deductions from statistics of cases gathered by various authors is the danger arising from utilizing the totals gathered by each and summing them up as so many individual cases; in this way a single case may be repeated and multiplied as many times as there are writers who sum up the cases.

Of the three parts of the duodenum in which primary carcinoma has been found, the weight of evidence is in favor of the second part being more frequently involved than the other portions. We must bear in mind in this connection that the *papilla Vateri* is situated in the middle part of the duodenum, that primary carcinoma of the common bile-duct at the ampulla, while uncommon, still occurs, and may give rise to an extension into the duodenum by contiguity. Unless careful examination of the structures involved is made, it would not be easy to say in what organ the tumor was primary. In this connection it might be well to point out that Rolleston[17] has shown that most of the so-called cases of carcinomata of the ampulla of Vater originate in the *termination* of the common bile-duct. One must differentiate between cancer of the termination of the common bile-duct, of the ampulla of Vater, and primary carcinoma attacking the mucous membrane covering the duodenal surface of the *papilla Vateri*, the last being a primary duodenal cancer, the former being much more common and coming under the classification of primary carcinoma of the biliary passages. Of the carcinomata of the middle portion of the duodenum, these circumpapillary carcinoma are the most frequent, and are especially prone to produce infections of the biliary ducts, as infective suppurative cholangitis and intrahepatic abscesses.

We should likewise exclude, in considering this topic, extension of carcinoma into the duodenum from other contiguous organs. Cases of carcinoma of the duodenum have been described as extending from the cæcum, ascending colon, transverse colon, the liver, the head of the pancreas, the gall-bladder, and the stomach.

Whittier[15] gives the location of the growth in 12 of the 13 cases he describes. The first and second portion of the duodenum was involved once, the second portion in 9 cases, the third portion once, and in 1 case the carcinomatous mass invaded the entire length of the duodenum.

In Pic's[16] 8 cases the location is given in 7, as follows: upper part of duodenum in 2, middle part in 4, and conjoined middle and lower portion in 1.

From Perry and Shaw's[2] report we gather that of 13 primary duodenal carcinomata 5 occurred in the upper part of the duodenum, 6 in the middle, and 1 in the lower part; the thirteenth case involved the entire length of the duodenum. It is curious to note here that in no case did the carcinoma extend through the pyloric ring into the stomach, a corollary to the fact brought out by Cuneo and Lucène[1] that pyloric carcinomata do not, as a rule, extend through the valve into the duodenum.

In 41 cases collected by Rolleston,[18] which probably include many if not all the cases of Perry and Shaw[2] and some of Nattan-Larrier's,[19] the first part was affected alone in 8, and together with the second part in 5 more; the second part was involved alone in 24 cases, and together with the first part in 5 as just stated, and the third part in 4. The third part is, therefore, the most infrequent as the seat of primary carcinoma. In this connection mention should be made of a very unusual case reported by Pye-Smith[20] of two distinct and separate carcinomata of the duodenum in one subject, the upper one involving the duodenum just beyond the pyloric sphincter, the other, the larger, occurring three inches lower down.

The Fenwicks[3] in their monograph on *Cancers of the Stomach and Duodenum* collected 51 cases of duodenal carcinoma, most probably including Whittier's, Pic's, some of Perry and Shaw's, Nattan-Larrier's, and Rolleston's cases, and found the following distribution: the upper third of the duodenum was involved in 11 cases, or in 21.5 per cent.; the middle third in 29, or in 57 per cent.; the lower third in 7, or in 13.5 per cent. In addition 8 of the cases involved the whole or the greater portion of the duodenum.

VARIETIES. In the great majority of the cases intestinal carcinomata are primary, very rarely are they metastatic. I have not come across the record of a single case of duodenal carcinoma which was metastatic in origin.

It is only within comparatively recent years that carcinomata were differentiated by histological differences. Early records of

duodenal carcinoma describe and differentiate them on the basis of their external appearances; thus the writers speak of them as soft or hard, fungoid or encephaloid, nodular or polypoid, and so on.

Regarding them from a histological point of view, the very large majority of duodenal carcinomata are of the cylindrical-celled variety, and show a glandular type, the so-called adenocarcinomata. A few cases have been reported of spheroidal-celled carcinomata, and their presence might raise the question as to whether such duodenal carcinomata were not extensions from the ampulla, from the *ductus Wirsungii*, or from the pancreas. According to the proportion of stroma to cells we have, on the one hand, when the stroma is abundant and the cells relatively few, the scirrhus form, and when the cells are in predominance and the stroma small in amount the medullary form. Both forms obtain in the cases reported. When the cells of the cylindrical-celled carcinomata of the duodenum undergo so-called mucoid or colloid degeneration they give rise to the gelatinous or colloid carcinoma of the duodenum. All forms are subject to retrogressive or necrotic change, whereupon softening and ulceration occur; in fact, these changes are common in duodenal carcinomata, and especially in those surrounding the *papilla Vateri*, and add to the disease picture a superimposed suppurative infection of the biliary passages and ducts or an abscess of the liver, as previously mentioned.

The tendency of growth is in an annular direction, more from the mucosa toward the lumen than into the underlying tissues of the mucosa, with the result that a more or less complete stricture of the duodenum occurs. Above the stricture dilatation takes place. Sometimes the stricture assumes a funnel shape. The spheroidal-celled variety grows more as a flat excresence with overhanging edges, and shows a greater tendency to ulcerate. The dilatation of the duodenum above the stricture may be very great, the walls of the dilated portion become thickened from hypertrophy of the muscular coat, and the mucous membrane shows the changes of a chronic catarrhal inflammation with superficial ulcerations.

Metastases are uncommon and, when they do occur, show themselves very late in the disease. Neighboring lymph nodes, it is said, are not often involved and likewise only toward the end of the disease.

Sex. Males form the preponderating majority of the victims of duodenal carcinoma. All of Whittier's[15] 13 cases were males; of Pic's[16] 8 cases, 3 were females. In the 43 cases tabulated by Rolleston[18] 33 of the patients were males and 10 were females.

Age. Victims of carcinoma of the duodenum are usually a little beyond the middle period of life. There seems to be a tendency for carcinoma to attack the small intestines a little earlier in life than does carcinoma of the other organs. The average age at which carcinoma of the duodenum occurs seems to be fifty-two years. Of

Whittier's[15] cases the youngest was seventeen years, two were eighteen years, and the oldest eighty-four; of Rolleston's[18] tabulated cases, 7 were seventy years or older, the youngest was twenty-seven, and the oldest was eighty.

DURATION. The Fenwicks[3] place the average duration of life of the individual attacked with duodenal carcinoma as seven months, the extremes in their review of the cases collected being three months and eighteen months.

SYMPTOMS. There is no doubt that there is a great difficulty in recognizing the disease during life. In fact, it is almost impossible to diagnose with certainty the disease when it attacks the upper portion of the duodenum, for then its symptoms are almost identical with those of pyloric carcinoma.

The symptoms will depend upon the site of the growth and its relation to the papilla of Vater; therefore, the symptomatology had best be given separately of the suprapapillary cases and of the infrapapillary ones. The cases of the juxtapapillary or circumpapillary variety present the picture of more or less complete obstruction of the common bile-duct, obstinate jaundice, cholæmia, and sometimes that of suppurative inflammation of the bile-ducts and multiple abscess of the liver. Their diagnosis, excepting as to probability, cannot be made, because their symptomatology does not sufficiently differ from carcinoma of the common duct, from carcinoma of the head of the pancreas, or from carcinoma of the ampulla of Vater. There occasionally occur rare exceptions to the rule of obstinate jaundice in the juxtapapillary or circumpapillary carcinomata, in which the jaundice may vary in intensity from day to day, and even entirely disappear for a time to recur shortly after. This is due to the fact that while the flow of bile is greatly interfered with it may not be completely blocked, and with the biliary *vis a tergo* increasing with the increasing pressure, the bile is finally forced through the obstructed opening of the papilla, or it may be that ulceration and breaking down of the growth may give rise to a reopening of obstructed channel. This seemed to be the case in a patient of mine,[21] who entered my wards at Mount Sinai Hospital on April 6, 1902, whose case was recorded by me in the *Mount Sinai Hospital Reports*, 1903, vol. iii. p. 49. In this case there was a carcinomatous growth lying at and around but not inside the papilla of Vater; it was annular, 8 cm. in diameter. The opening in the papilla was not entirely obstructed, but the orifice was overlapped by the growth; the pancreatic duct was much dilated and opened directly into the duodenum ½ cm. below the opening of the papilla of Vater, instead of joining with the common bile duct, which is the rule, to form the ampulla.

There was a complete obstruction of the orifice of the pancreatic duct by the growth, which proved to be an infected adenocarcinoma.

In all varieties the most pronounced symptoms are gastric, and similar to those of pyloric carcinoma, such as loss of appetite, eructations, nausea and vomiting, signs of increasing starvation, with its accompanying loss of strength and loss of weight; there are also abdominal pain and increasing cachexia. The pain is for the most part in the right hypochondrium, often in the epigastrium, and occasionally extends over the entire upper abdomen.

A tumor is often palpable in all varieties, though just as often one is not to be felt. When it is palpable it is situated in the right hypochondrium near the middle line of the body. It is slightly movable when the carcinoma is in the horizontal superior part of the duodenum; immovable when it occurs in the descending and in the inferior horizontal part, owing to the fixed connection of the latter two parts to the posterior abdominal wall.

Constipation, while it exists for the most part, is not a marked feature of the disease. It may be entirely absent or it may alternate with diarrhœa.

The abdomen is, as a rule, flat and even at times retracted or sunken.

The urine is diminished, the amount of chlorides diminished and occasionally entirely absent, and indican is often present in large but varying quantity.

The vomitus is very large, sometimes as much as seventy to eighty ounces, as one would expect to find in interference with gastric motility. Sometimes there is hæmatemesis, or vomiting of blood changed by the duodenal and gastric secretions—coffee-ground vomit. Persistent vomiting of bile is the distinguishing feature of carcinomata situated below the papilla Vateri. In all varieties the vomiting is recurrent.

Juxtapyloric or Suprapapillary Carcinoma of the Duodenum has all the subjective symptoms of the other forms. It has neither subjectively nor objectively any localizing signs which would suggest a prompt, even a probable diagnosis. Its chief subjective symptoms indicate a severe disturbance of gastric motility.

The objective signs are more important; the earliest is a tumor, more or less tender to the touch, painful, even independent of pressure. The tumor appears in the right hypochondrium near the median line; it is only slightly movable, if movable at all. Owing to the tendency of the growth to encircle the bowel and to produce a stricture, dilatation of the duodenum and the stomach result. The signs of gastrectasis develop, and gastrosuccorrhœa, with vomiting of large quantities of fluids, supervenes.

A tumor is not always palpable, and the signs of interference of gastric motility suggest most often the diagnosis of pyloric stricture or neoplasm.

The physical examination of the stomach contents will throw no light on these cases, although it is stated that the presence of free

hydrochloric acid in a case showing the signs of a pyloric carcinoma might suggest a diagnosis of juxtapyloric carcinoma of the duodenum. Boas observed a case in which the presence of free hydrochloric acid was demonstrated from the contents of a much distended stomach, and in which, owing to the absence of a palpable tumor, a diagnosis of benign stenosis of the pylorus was made; a laparotomy disclosed a neoplasm in the first portion of the duodenum. Boas[22] says we must not lay too much stress upon the results of chemical examinations, since free hydrochloric acid is often present for a long time in carcinoma of the pylorus, and, on account of the stagnation which results from proximity to the stomach, it may be absent and lactic acid present in duodenal carcinoma.

Czygan[23] called attention not long ago to the presence of splashing sounds between the tumor and free border of the ribs, and attributed them to the contents of a much-dilated duodenum. On removing the contents of the stomach the sounds disappeared, to reappear when that viscus was again filled. He insists that this sign is an important aid in arriving at a diagnosis.

Circumpapillary Carcinoma of the Duodenum. As we have shown, the descending portion is the most frequent site for carcinoma to affect the duodenum. When situated above the papilla its symptoms are similar to the juxtapyloric cases; when it involves the papilla it necessarily causes an obstruction to the flow of bile and jaundice develops. Jaundice is, therefore, the prominent sign. The jaundice is usually permanent, though in a few cases it has been absent entirely, the bile-duct not being obstructed; it has been intermittent or it has varied in intensity from day to day in still other cases. The subjective symptoms are indefinite and in themselves are of very little service in suggesting a diagnosis.

The objective symptoms are similar to the other forms of duodenal carcinoma plus the jaundice. A tumor is rarely felt, and in the cases in which a tumor could be palpated it was fixed and immovable in the right hypochondrium.

Jaundice comes suddenly and without pain, though in my case sharp pains preceded the development of jaundice, resembling an attack of cholelithiasis. Should signs of sepsis and tenderness over the liver follow, showing an infective process in the bile-ducts, one should bear in mind that such sequelæ may follow an ulcerating infected carcinoma of the duodenal papilla as well as an infection of the biliary passages due to a stone. If added to these symptoms obstinate vomiting, melæna, cachexia, and rapid loss of weight appear, a suspicion of juxtapapillary duodenal cancer might be formed. However, an absolute differentiation from carcinoma of the head of the pancreas is beyond clinical methods.

Infrapapillary, Juxtajejunal or Prejejunal Carcinoma of the Duodenum forms the smallest number of duodenal carcinomata, but comprises the cases in which occasionally a diagnosis

is possible. The diagnostic feature is contained in the vomit. Leichtenstern was the first to call attention to persistent vomiting of bile as the distinguishing feature of infrapapillary carcinoma. Pic[16] says Chomel[24] had previously, in 1852, called attention to this point. There is no doubt that in cases of duodenal stricture biliary vomiting is a marked feature. The stomach contents, even when there is no vomiting, or before vomiting occurs, will show the presence of bile.

For the same reason that bile is regurgitated into the stomach, the pancreatic secretion finds its way into that viscus. Should an examination of the contents of the stomach demonstrate the presence of the proteolytic ferment, trypsin, a diagnosis of obstruction below the biliary papilla may safely be made; when the other signs denoting a malignant disease are present a diagnosis of infrapapillary carcinoma of the duodenum would be justifiable. One must bear in mind, however, that the permanent presence of bile in the stomach contents alone is not sufficient to justify a diagnosis of prejejunal stricture, because in cases of gastrobiliary fistula bile is likewise to be found in the stomach. There must be associated the signs of lost gastric motility, the presence of trypsin, and the usual signs indicating malignant disease to justify the diagnosis of infrapapillary stricture due to malignant neoplasm.

Treatment. For the cure of these conditions therapeusis is of no avail. Whatever means we possess, whether medical or surgical, are merely palliative. Yet in surgical interference it would be well to bear in mind that in carcinoma of the first portion of the gut, if the technical difficulties be not too great (that is a question the surgeons must decide) a resection of the pylorus and affected portion of the duodenum might give some promise of a cure, because carcinoma of that portion very rarely extends beyond the pylorus, metastases appear only very late in the disease, and the neighboring lymph nodes are involved likewise very late. For carcinoma resulting in stricture of the other portions a gastroenterostomy may prolong life for some time. What hope of success would follow excision of the third portion of the duodenum when it is the seat of disease remains to be seen.

Thus far the only operation suggested as giving temporary relief has been a gastroenterostomy.

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PSEUDOLEUKÆMIA GASTROINTESTINALIS.

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Pseudoleukæmia, in which the lymphatic apparatus of the gastrointestinal tract is the seat of the principal lesions, has been rarely reported. In a somewhat extended review of the literature of pseudoleukæmia, under its various synonyms, with the view of

determining the frequency and extent of the lesions in this location, 238 cases have been found which came to autopsy. In 204 of these cases the gastrointestinal tract was recorded as normal, or was not mentioned, and therefore was probably not greatly, if at all, affected. Of the remaining 34 cases, 1 in 7 of the entire number, conditions varying from slight swellings of the mucous membrane and lymph follicles to extensive hyperplasia of the lymphoid tissue of the whole alimentary tract were found. In 15 cases the condition was confined to the intestines, while the stomach was affected seven times. In the remaining 13 cases both stomach and intestines were extensively infiltrated. In but 7 did the condition approach that found in the case we have to report.

Murchison, writing in the *Transactions of the Pathological Society of London* as early as 1869, recognized these peculiar conditions, and under the name of lymphadenoma presented a case which was in all probability lymphosarcoma, and which he reported as differing from any which he had met with or seen described, although Briquet, thirty years earlier, had described one of the most striking cases on record, which was also beautifully illustrated in Cruveilhier's *Atlas*. In 1884 Carrington reported a similar case, and considered the condition one of very great rarity, having found in the records of the Pathological Society and other sources but four cases resembling his, including Murchison's case. Again, in 1889 Pitt described these four and an additional one which had come under his own observation. Hadden reported his case as very unusual, having seen no other case in which the intestines were affected in "lymphosarcoma." Rolleston classified his case with Pitt's. In an extensive report in 1897 by Schlesinger on sarcoma of the stomach was reported a case as *pseudoleukæmia intestinalis*, and this case is also included in a series of four cases recently reported by Stoerk, three of which he had personally observed, and to which he gives the name of "pseudoleukæmia intestinalis or lymphosarcoma of the stomach." Seven cases presenting the most extensive gastrointestinal lesions have been selected and arranged chronologically in the following series:

CASE I. (Briquet, 1838).—Male, aged forty-one years, with a clinical history of swelling of the testicles, inguinal region, and neck. Apparently the beginning was an inflammation in the mouth. This case is illustrated in Cruveilhier's *Atlas* (1839). The following findings were recorded: Mucous membrane of the mouth pale; at the base of the tongue the lymph follicles were greatly enlarged, and the tonsils were double their normal size. Trachea, larynx, and œsophagus normal. The stomach was of normal size, but its mucous membrane, which was pale throughout, was thrown into heavy, sinuous folds like cerebral convolutions, these folds terminating a short distance from the pyloric orifice; the other membranes of the stomach were normal. The mucous membrane

of the small intestine was gray and of normal consistence, but the surface was covered with a great number of polypoid growths, single and confluent. These were enlarged lymph follicles. These growths differed in appearance, some forming flat patches, while others were pea-sized and polypoid in form. In the upper part of the small intestine these growths were numerous, and in the lower half they were of a smaller size, but still more numerous. The Peyer patches were also enlarged and swollen near the ileocæcal valve, which itself was greatly enlarged, purple in color, and covered with miliary follicles. In the large intestine the follicles were very numerous, as large as the point of the little finger, polypoid and sessile, the mucous membrane being normal. The vermiform appendix was as thick as the thumb, and consisted of large follicles. The muscular and serous coats of the intestinal tract were normal. The lymphatic glands of the abdomen were greatly enlarged, as also were the spleen and liver. The kidneys and bladder were normal, and the prostate was greatly enlarged. No examination of the blood was made.

Case II. (Carrington, 1884).—A woman, aged fifty-five years, with enlarged cervical glands and a history of wasting for six months, without abdominal symptoms. At autopsy the cervical glands were found large and fleshy, as also were the mediastinal glands and the mesenteric glands. A large mass of glands pushed up the root of the mesentery and surrounded the pancreas. All the lymph glands were enlarged, especially in the portal fissure and the groin. The peritoneum was healthy. The stomach was studded over its mucous surface with very numerous cream-colored, flattened tumors; these were of mixed size, and some a little ulcerated. "Many of them were more infiltrations of the wall than distinct tumors; many, again, not even infiltrations, but conversions of the actual texture into new material." The pylorus was invaded by the same cream-colored growth, and was thrown into loose folds thereby. The duodenum was practically healthy, but below this the mucous membrane began to show disease. The valvulæ conniventes, here and there, first became swollen and firmer than natural, then polypoid and creamy. Sometimes a smaller or larger flattened swelling of the valvulæ occurred, with a little ulceration in the centre. This condition extended throughout the small and large intestine, but was more marked in the latter. The solitary glands and Peyer's patches were enormously enlarged, so as to constitute cream-colored, fleshy plates upon the surface of the mucous membrane. A few inches above the ileocæcal valve one growth of this kind measured one and one-half inches in diameter and half an inch in thickness. There was enormous thickening of the mucous membrane covering the ileocæcal valve, forming a thick fold surrounding the valve, of about half a pound in weight, which distended the cavity of the cæcum. There was neither con-

traction nor dilatation of the bowel in any part. The spleen weighed forty-four ounces. On section it showed a diffuse soft growth throughout, modelled on the normal pattern and color, so that the surface seemed to show enormous Malpighian bodies. The liver was normal. The blood count showed 4,720,000 reds and 4.3 whites to 1000 reds.

Case III. (Hadden, 1887).—A man, aged fifty-four years, with abdominal tumor and great emaciation. At autopsy a large tumor was found in the abdomen, involving the mesenteric and retroperitoneal glands; the axillary, inguinal, cervical, and iliac glands were also affected. There was a solitary nodule of growth in the liver. The spleen was large, measuring 10 x 5 inches, and studded with dull-white nodules. Near the pyloric orifice of the stomach there was one small, raised nodule of growth about one-third of an inch in diameter, apparently arising in the submucosa. All the intestinal glands, solitary and agminated, from the duodenum to the rectum, were much enlarged, elevated, and firm. This enlargement was very marked in Peyer's patches, and in the ileum near the valve the masses were enormous. The growth was strictly limited to the glands, and there were no ulcerations. Microscopically the hyperplasia of round cells was found localized to the glands without invasion of the surrounding parts.

Case IV. (Pitt, 1889).—The patient, a male aged forty-eight years, had gradually emaciated during the nine months preceding his death, but there were no symptoms of abdominal disease noted until the autopsy. At the base of the tongue were found three lymphoid masses, and there was a marked hypertrophy of the tonsils; the glands at the bifurcation of the trachea were large and swollen. There were enormous masses of lymphoid overgrowth on the mucous wall of the stomach, forming large, sessile tumors. At the cardiac end, two inches from the œsophagus, were large masses, both sessile and polypoid, one of which was $2\frac{1}{2}$ x 2 x 1 inch in size. Others occurred as raised vermiform overgrowths ramifying over the surface, of the thickness of a little finger. Over the greater portion of the body of the stomach there was also less extensive lymphoid growth, occurring in small, raised, flat patches of varying sizes. On the larger curvature, one and one-half inches from the pylorus, was a flat mass of growth one and one-quarter inches across, with a cupping of the surface which also occurred to a less extent in several of the other growths. The growths were all creamy-white in color, very soft and succulent, and the largest masses were breaking down at their bases. The mucous membrane was not ulcerated. In the duodenum immediately below the pylorus were numerous raised lymphoid growths about one-third of an inch across, stained slaty black. The whole of the small intestine was dotted with many thousands of raised polypoid growths about the size of large peas, scattered singly about, and there were flat

plaques of growth in Peyer's patches, which were raised about one-sixth of an inch; many of these growths were superficially ulcerated. There were large masses of growth along the ileocæcal valve, and the orifice of the vermiform appendix was occupied by a pigmented polypoid mass the size of a large chestnut. In the colon there was no lymphoid overgrowth. The mesenteric glands were universally swollen and enlarged. The spleen weighed 25.5 ounces, soft, and showed a general hypertrophy of the Malpighian bodies. The liver and kidneys were normal. No blood count was made.

CASE V. (Schlesinger, 1897).—In his study upon sarcoma of the stomach, Schlesinger reports a case diagnosed during life by a nodule taken from the rectum, showing histologically what was considered a lymphosarcoma. The spleen and lymph glands were enlarged. Death was from facial erysipelas. Autopsy was performed by Prof. Kolisko, who made the diagnosis of *pseudoleukæmia intestinalis*. The patient was a male, aged sixty-two years. The spleen was three times its normal size, firm and bloody, with the follicles enlarged to pea size. The mesenteric lymph glands of the ileum formed immense tumors, were marrow-like, soft, and white. The mucous membrane of the entire intestinal tract was pigmented gray, and from the pylorus to the ileocæcal valve was covered with flat infiltrations standing out in patches, also of marrow-like consistence. In the entire large intestine were patches and polypi corresponding to the solitary follicles. The mucous membrane of the appendix was a finger thick, and of the same soft nature. The stomach and pylorus had polypoid infiltrations and sinuous folds. The mucous membrane was also thickened in masses. All the other abdominal glands were enlarged and soft. The blood count showed 2,100,000 red corpuscles, hæmoglobin, 55 per cent., and "few leukocytes."

CASE VI. (Herrick, 1898).—A male, aged fifty years, was in the Cook County Hospital one and one-half years with all the glands, especially the cervical glands, enlarged. Attacks of erysipelas were followed by decrease in the size of the swellings. Death from exhaustion and dyspnœa. Autopsy by Prof. Hektoen. Enormous tumor masses were found in the neck and mediastinum, causing pressure upon the œsophagus and trachea. The nares and pharynx were filled with nodules, and the tonsils met in the median line. Tumor masses infiltrated the lungs, and the spleen showed one, but there were none in the kidneys and liver. General enlargement of the lymphatic nodules, Peyer's patches, and solitary follicles of the entire alimentary tract. The cæcum was filled with hard, blackish nodules, and masses attached to the wall of the intestine, while the vermiform appendix was thicker than a man's thumb, its lumen being filled with hard nodules and its opening into the cæcum occluded. The œsophagus contained many enlarged follicles. The mucous membrane of the stomach was the seat of a

universal diffuse invasion with these soft, white nodules, especially in the fundus, where the mucous membrane was thrown into large folds. The lymph glands throughout the body were greatly enlarged, and the pancreas was embedded in a mass of them.

CASE VII. (Stoerk, 1904).—A woman, aged fifty-seven years, with a history of diarrhœa alternating with constipation, bloody stools, great abdominal pain, and œdema. At autopsy the lymph follicles at the base of the tongue and the tonsils were considerably enlarged. Cervical, mesenteric, retroperitoneal, and inguinal glands were all enlarged, and on the cut surface showed a gray-white, homogeneous appearance. The spleen measured 16 x 10 x 4 cm., flabby, with enlarged Malpighian bodies. The stomach was greatly dilated, and showed a peculiar stiffness of the wall. On opening the stomach the mucosa showed a very great thickening of the folds, running lengthwise. These folds were eroded at the summit, and showed some ulceration. In many places between the folds of the mucosa were white nodules the size of a pea, with melanotic discoloration. The pylorus was involved in this condition, and the duodenum to a less extent; the folds were increased in size, and contained prominent lymph follicles. In the small intestine the same condition was present, and Peyer's patches were enlarged. In the large intestine the mucous membrane was very much thickened and covered with numerous enlarged, single, discolored follicles. Especially remarkable was the condition in the colon, decreasing from the cæcum toward the anus. The bone-marrow was deep red, soft, and moist. Microscopically a very slight infiltration of round cells was found in the kidney and liver. The blood count showed: lymphocytes, 41.2 per cent.; large mononuclears, 4.6 per cent.; eosinophiles, 1 per cent.; neutrophiles, 53.2 per cent., and a few myelocytes.

Rolleston and Latham report a case somewhat similar to that of Pitt's, with much hyperplasia in the stomach, but not in the intestine, and not well generalized in the lymph glands. However, the blood showed evidences of splenomyelogenous leukæmia, and, as the authors are in doubt as to its proper classification, it has seemed best not to include it in this series. There is much reason to believe, however, that this case is of the type that has sometimes been reported as an instance of pseudoleukæmia becoming transformed into leukæmia.

CASE VIII.—On November 17, 1903, the following typical case of pseudoleukæmia gastrointestinalis was examined post-mortem at the Chicago Baptist Hospital: E. H., a minister, aged fifty-one years, was admitted to the service of Dr. J. P. Webster, to whom we are indebted for the privilege of reporting the history of the case, kindly furnished by the house physician, Dr. Adams. He was a strong, athletically inclined man, who had been well until the preceding winter, when he complained of "feeling as if he were going to be

sick." This feeling persisted through the spring. In April he caught cold, and was confined to his bed for six weeks with a severe bronchitis, from which he was not expected to recover; he had high fever and night-sweats. He gradually recovered from this illness, but never again became perfectly well. He became anæmic, and in October began to have night-sweats. Fresh air and dietetic treatment had little beneficial effect. Massage was tried, first of the limbs, and then of the stomach and bowels, on account of "poor digestion." Vigorous massage over the stomach caused a feeling of "goneness." In September he took a trip through Iowa, during which his health failed rapidly. He was told that he had kidney trouble, and took some proprietary treatment for it, but this disturbed his stomach so much that he was forced to give it up. At this time he complained of "grabbing pains" in the region of the stomach, and jerking of the limbs. At this time urinalysis was made, and nothing abnormal found. On admission to the hospital for an exploratory laparotomy, which had been recommended, examination revealed the following condition: The patient was anæmic, temperature normal, pulse from 90 to 100. The lungs showed signs of a slight bronchitis, and the heart was negative. Abdomen very tense and tympanitic, and tender on deep pressure over the stomach. With some difficulty a tumor mass about the size of a man's fist was outlined by percussion and palpation, corresponding in position to the region of the pylorus. The lymph glands were enlarged all over the body, varying from pea to almond-size.

Urinalysis was negative. The diagnosis that was made lay between carcinoma of the pylorus and tuberculous peritonitis without effusion.

On opening the abdomen for the purpose of laparotomy the stomach was found greatly dilated, and its wall thickened from pylorus to cardia; the duodenum also seemed to be thickened. Gastroenterostomy was performed, uniting the upper part of the jejunum to the lower posterior part of the stomach by means of a Frank button. When the stomach was opened the organ did not collapse, because of the diffuse thickening of the walls, and the rugæ were found to be as thick as the finger. A piece of the mucous membrane and one of the enlarged mesenteric glands were removed for microscopic examination. As was to be expected, the diseased organ did not react well to the operative procedure; leakage occurred about the button, and death occurred eleven days later from peritonitis. Unfortunately, at no time during the patient's illness was a blood examination made.

The tissues removed at the operation were sent to the Pathological Laboratory of the University, and the diagnosis of "pseudoleukæmia, with hyperplasia of the lymphatic apparatus of the stomach" made on the histological findings.

Autopsy was performed five hours after death, and the report upon the findings is as follows:

Anatomical Diagnosis. Pseudoleukæmia; general lymphadenoid hyperplasia, particularly of the alimentary tract and peripancreatic glands, with resulting enlargement of stomach and appendix; diffuse acute suppurative peritonitis; recent laparotomy wound, infected; anastomosis of stomach and duodenum by suture and Frank button; hyperplasia and hyperæmia of red bone-marrow; hyperplasia of Malpighian bodies of spleen; parenchymatous enlargement of liver and kidney, with lymphoid infiltration; sclerosis of coronary arteries (minimum degree); apical, fibrous pleuritis; hypostatic congestion, bronchopneumonia, and œdema of lungs; fibrous perisplenitis.

External Appearances. Body of a tall, slender, poorly nourished man, 175 cm. in length. Body not entirely cold, having been dead but five hours. Rigor mortis present. Sclera white. The skin is pale. In the median line of the abdomen is a long operative wound (gaping), 18 cm. long. The floor and walls show a purulent fibrin. The floor of the wound is formed by the parietal peritoneum and by the intestine bulging through the peritoneum. The muscle on the sides of the wound is pale and wax-like.

Abdominal Cavity. The intestines are everywhere matted together by easily torn, fibrinous adhesions. The cavity contains about one litre of thin, yellow, opaque, purulent fluid. Between the stomach and the diaphragm on the left side is a collection of thick, yellow, purulent material. The stomach is distended and also the intestines to a moderate degree. The peritoneum is covered with a thin layer of fibrin. Between the folds of the intestines drops of pus are found. There are no adhesions between the liver and the diaphragm, but a few about the spleen. Every other part of the peritoneal cavity is obliterated by adhesions.

Pleural Cavity. Lungs meet in the median line. On the left side are a few fibrinous adhesions at the apex; pleura smooth. No other changes.

Pericardial Cavity. Pericardium smooth and shining, free from adhesions. The cavity contains about 50 c.c. of clear, serous fluid.

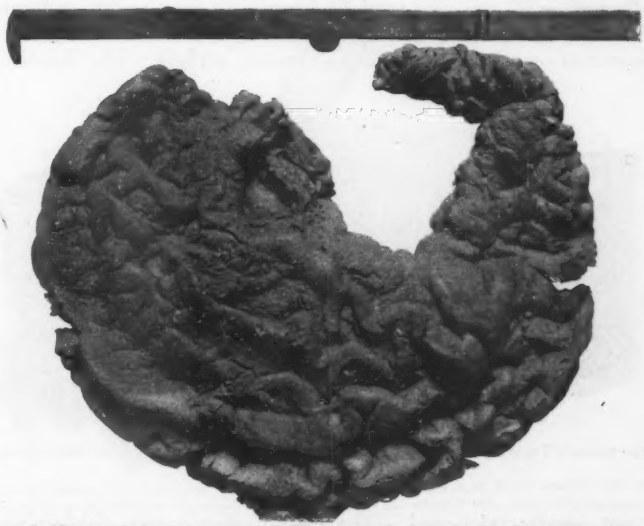
Thyroid and Thymus. The fat at the site of the thymus shows evidence of some lymphatic tissue.

Heart, Aorta, and Vessels. The heart is of normal size. The coronary arteries are tortuous. There is a considerable amount of fat. The ventricles contain large, soft, pale clots. The anterior coronary artery has slight patches of thickening. The aortic and pulmonic valves show no change. The myocardium is firm and of normal color. The tricuspid orifice admits five, the mitral orifice admits three finger-tips. The mitral and tricuspid valves show no change. The foramen ovale is closed; the endocardium is normal.

Lungs. The right lung has few adhesions between the lobes. The posterior is heavier than the anterior and darker. At the apex are a few hard, fibrous nodules. The upper lobes contain considerable fluid. The dark parts of the lower lobe crepitate but little and contain a bloody, frothy fluid. The left lung is the same as the right, except that the dark area is smaller. At the hilum are also small, hard glands.

Liver. The liver is enlarged, measures 28 x 21.5 x 17 x 11 x 6 cm., and weighs 2470 grams. The enlargement is diffuse. The external surface is roughened, as if each lobule is enlarged. Beneath the

FIG. 1.



Lymphoid hyperplasia of the stomach. The stomach is shown in this illustration inverted, to show the enormous thickening of the rugæ, and on account of the thickness of the walls is thereby made somewhat smaller than when in its natural condition. The stomach wall weighed 1300 grams—nearly as much as a normal liver.

capsule there are numerous pale, slightly elevated areas, that do not penetrate the liver substance. The consistence is slightly increased. Individual lobules are enlarged and much lighter than normal, except in the centre.

Spleen. This is slightly enlarged, weighs 160 grams, and is of normal consistence. The cut surface shows the Malpighian bodies much enlarged and prominent. Pulp has but little blood, and is not softened.

Pancreas. The pancreas is of normal size and shows no gross changes, although a string of greatly enlarged glands lies along the upper border.

Gastrointestinal Tract. The stomach is enormously enlarged, and weighs 1350 grams when empty. Along the attachment of the omentum are numerous pea-sized lymph glands. When cut open it does not collapse, because the walls are much thickened. This thickening is fleshy, diffuse, yet nodular in places, and the thickness of the opposed walls together is from 4 to 5 cm. The rugæ are much swollen, and in places form tumor-like masses about 2 to 4 cm. thick. These are soft, being about the consistence of the large soft lymph glands. The thickening involves every part of the stomach, and is greatest about the pylorus. A Frank button is found in a sutured opening between the duodenum and stomach. The entire length of the stomach along its greater curvature when collapsed is 57 cm.; its straight length, 33 cm.; width, collapsed, 13.5 cm.; thickness, 5 cm. by external measurement. There is no ulceration or other change in the mucous surface. The duodenum

FIG. 2.

Hyperplasia of Peyer's patches and solitary follicles of the small intestine in pseudoleukæmia gastrointestinalis.

is not greatly thickened. The cæcum shows great thickening of the wall, which is reddish, and resembles the stomach, the greatest thickening being at the beginning of the appendix, where there is a mass 4 cm. in diameter. The solitary follicles and Peyer's patches are thickened, raised, pigmented, and slate-colored. The change is more marked toward the lower end. The whole intestine weighs 1500 grams, and shows similar thickening of the lymph follicles. The lower end of the ileum shows Peyer's patches greatly enlarged, some measuring 7 x 3 cm. and being 8 mm. thick. The solitary follicles are slate-colored. The mucosa is a little thicker than normal. Farther up the enlargement of solitary follicles decreases, although Peyer's patches are all enlarged.

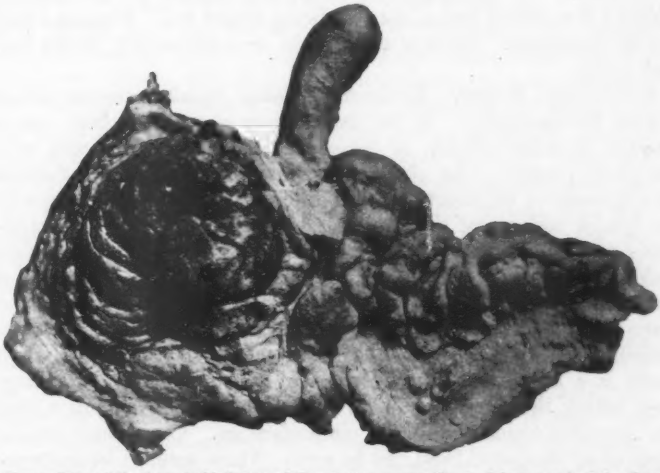
The appendix is solid in all its extent. It is 8 cm. long, adherent by its tip. It is larger toward the tip, where its circumference is about 57 mm. It has a mesentery about one-half its length, in

which are numerous lymph glands 5 mm. in diameter. The enlargement is solid and uniform, the consistence that of the normal appendix. The lumen seems open. The mesocolon is swollen and reddened. The mesentery is very friable.

Adrenals are of normal size. The cortex seems thicker than normal, and is pale and solid.

Kidneys. Their combined weight is 400 grams. The right kidney is a little enlarged. The consistence is normal. The cortex is thickened, measuring 7 x 10 mm. It is generally pale, and the cortical markings are obscure. The capsule strips easily. The left kidney is the same as the right.

FIG. 3.



Hyperplasia of the lymphoid tissues of the cæcum, appendix, and lower end of the ileum. The orifice of the canal of the appendix can be seen in the summit of a tumor-like mass in the cæcum. In the ileum is seen an enlarged Peyer's patch.

Urinary Tract. The urinary bladder is not thickened. The prostate is not enlarged.

Generative Tract. The testicles appear normal.

Lymph Glands. The suboccipital glands are not palpable. The posterior cervical glands are 0.5 x 1 cm. in size. The submaxillary glands are twice the normal size. The glands beneath the sternocleidomastoid and about the clavicle are not palpable. The axillary glands are much enlarged on both sides, about the size of cherries; those at the elbow are not palpable. The inguinal and femoral glands on both sides measure from 1 to 1.5 cm. in diameter. The glands at the hilum of the lung are large, soft, and anthracotic. In the posterior mediastinum is a group of glands measuring altogether 1 cm. by 5 cm. None of them is calcified or caseous. At

the attachment of the stomach to its ligaments are many enlarged, pale glands. The peripancreatic glands are enormously enlarged, the largest being 35 mm. long, very soft, pale, with small hemorrhagic spots. The retroperitoneal lymph glands are much enlarged. At the hilum of the liver the lymph glands are enlarged, soft, and pale. Lymph glands of the anterior mediastinum are not prominent; those of the neck and behind the clavicle are enlarged, flesh-like in consistence, pinkish in color. Some are deep red. The mesenteric lymph glands are enlarged, averaging about twice the normal size. The mesentery and omentum are everywhere studded with lymph glands. In the mesocolon are many dark-red lymph glands.

Skeleton. No changes except that the marrow of the clavicle shows a few yellow areas, the rest being bright red. Femurs could not be examined. Marrow of sternum very abundant, bright red, and pulpy.

Histological Report. Mediastinal Gland (small, measures about 5 mm. in diameter). In the fatty tissue about the gland are a number of small islands of lymphoid tissue, not connected with the gland proper. The gland under low power presents a normal arrangement of its structures, but differs from normal in that both the lymph nodes and the sinuses are much enlarged. The capillaries are all considerably distended with blood. In the lymph nodes the germinal centres are not distinguishable. The cells of the nodes are of the usual small round type, but there are many more pale nuclei than usual; karyokinetic figures are not abundant, although occasionally seen. The only unusual cell type in the lymph nodes is a frequently found form that consists merely of a large ring, taking the nuclear stain at its periphery only, and in a very few granules found within its circumference. Occasional similar types of an elongated form can be seen. These seem to be hydropic nuclei of germinal cells. The sinuses are crowded with a great variety of cells, of which the most abundant are large endothelial cells, lymphoid cells, and plasma cells. Polymorphonuclear leukocytes are present, but in small numbers. Eosinophiles are occasionally found, generally just outside a lymph node, although they do occur free in the sinuses; a few of them have nuclei resembling those of the plasma cell. The most striking features of the sinuses is the great number of plasma cells. In some fields they form by far the majority of the cells present, and in the sinuses, as a whole, are equal in number to either the lymphoid or endothelial cells. They often tend to group themselves together in nodules as large as the field of a $\frac{1}{12}$ inch objective, with but few other cells among them. A few mast-cells are found, much less abundant than the eosinophiles. There are not a few red corpuscles also present in the sinuses. Phagocytosis is not a prominent feature, yet large endothelial cells are frequently found containing various other cells,

especially red corpuscles, and lymphocytes, and frequently plasma cells. No giant cells were found.

Pancreatic Lymph Gland (largest gland in the body). Here the ordinary structure of a lymph gland is entirely lost, it being impossible to recognize any of the normal anatomical structures. The gland consists merely of a mass of cells of various sorts, in differing proportions in different areas, held together rather loosely. The bloodvessels are not numerous, and the lymph sinuses cannot be recognized. Occasionally small areas of necrosis are found, irregularly defined, and often containing many normal cells. Standing out prominently are small groups of very deeply staining nuclei located particularly at the periphery of the gland, but not distributed regularly. The predominant cell in this gland is one with a nucleus slightly larger than that of the ordinary lymphoid cell, usually round, but varying much in size and shape, the nucleus usually staining very deeply, but all degrees of staining are present, from nuclei nearly a solid black to those only staining at the periphery. These cells have very little cytoplasm, but occasionally have a double nucleus. Mitotic figures are abundant in them. They are distributed everywhere in the gland without any definite arrangement. In contradistinction to the small glands, plasma cells and eosinophiles are absent. Large phagocytic endothelial cells are abundant, and usually present abundantly in ill-defined areas, which probably represent the original sinuses of the glands. They are generally packed with cells, the most common of which have a single small nucleus, staining intensely in some, but in many the staining affinity for hæmatoxylin has been replaced by affinity for eosin. Red corpuscles are also often present in the phagocytes, and they are also quite numerous, lying free among the cells. All sorts of nuclear degeneration are present, and nuclear fragments, pyknotic and vacuolized nuclei are very abundant, as well as nuclei that have lost their affinity for basic stains. A very few cells contain yellow pigment granules. Polymorphonuclear leukocytes are very few in number.

Lymph Glands in General. Lymph glands of a size intermediary between these two, which represent extremes in this case, show changes corresponding to the relation in size to either extreme. The early changes seem to be chiefly a proliferation of lymphoid cells in the nodes, and of plasma cells in the medullary cords. Later the lymphoid cells overrun everything, and show at the same time both proliferative and retrogressive changes going on side by side, recalling the old distinction between leukæmia and pseudoleukæmia, in that in the latter "the gland cells proliferate but do not leave the glands." The plasma cells, and also the eosinophiles, disappear in the later stages. Giant cells of the type described by Reed are very scanty, not averaging more than one in a section, and are most numerous in the glands in intermediary stages.

Stomach. The great thickening of the wall is due to an enormous enlargement of the lymphatic structures of the stomach wall. Where a follicle normally existed is a mass of lymphoid tissue often 5 to 7 mm. in diameter, while between these nodes a diffuse proliferation of similar tissue has thickened the mucosa uniformly to a width of 3 to 5 mm. Occasional microscopic accumulation of lymphoid tissue is present between the layers of the muscularis, but the proliferation in every instance respects the connective and muscular layers of the stomach, never penetrating them to invade the deeper layers. There are, however, a few round cells and polymorphonuclear leukocytes between the muscle fibres. As the surface epithelium is not present in the specimens, it cannot be positively determined whether the lymphoid tissue has reached the surface or not, but the indications are that it seldom if ever passes beyond the basement membrane of the surface epithelium. There are no evidences of ulceration or infection. The structure of the proliferating tissue is quite the same as that of the lymph glands. Plasma cells and eosinophiles are abundant, particularly near the surface, while the central part of the new tissue is chiefly small round cells. Phagocytes are not abundant.

Intestines. A hyperplasia of all the lymphatic structures of the intestine is present, similar in all respects to that of the stomach. The growth respects always the surrounding tissues, and there is no ulceration. Not only are the solitary and agminated follicles enlarged, but small islands of lymphoid tissue seem to develop at frequent intervals. The chief difference from the stomach is that outside of the follicles there is not the diffuse lymphoid hyperplasia of the mucosa, so that the wall is not so universally thickened.

Œsophagus. Numerous areas of lymphoid tissue are found, particularly about the deeper glands, but there are none of any very great size.

Spleen. To the naked eye sections of spleen present a striking appearance, because of the deep stain of the Malpighian bodies in contrast with the pulp. Microscopically the changes are quite different from those in the lymph glands. The Malpighian bodies are generally larger than normal, and consist of two zones, a central mass of nuclei staining dark blue, and a peripheral zone of lighter staining, but more densely packed cells. The arteries within the Malpighian bodies are hyaline, and within the bodies are often present also masses of homogeneous material, arranged in bands, and staining intensely with eosin. This material is not found in all the bodies, and never in the pulp. The cells in the centre of the bodies are almost solely the deep staining mononuclear cells, which show neither mitosis nor degenerative changes. There is much increase in the amount of pulp. Red corpuscles are found in contact with the hyaline masses, but not elsewhere. The outer zone of the bodies consists of cells with elongated nuclei and a small

amount of cytoplasm; there are appearances that suggest that these cells are derived from the round cells. In this zone plasma cells are abundant. The pulp is very different from normal, consisting of broad bands of cells with considerable cytoplasm and little intercellular substance, forming a meshwork in the interstices of which red corpuscles are found. These bands seem to be formed by proliferation of the cells of the spleen sinuses of the endothelial type, although there are also very many plasma cells, and frequent eosinophiles and lymphoid cells. There seems to be much filling up of the spleen sinuses by these proliferated cells, which frequently contain granules of golden pigment, and occasionally red corpuscles and lymphoid cells. The total amount of blood in the spleen is small. By Van Gieson's stain there is no increase of material taking the red stain anywhere in the organ.

Thymus. This organ seems to have largely escaped the general lymphatic hyperplasia, for it contains no more lymphoid tissue than is often found in adults, although probably more than is usually found in men of the age of fifty-one. The largest nodes are the size of a pinhead, and consist almost solely of small lymphoid cells. The appearances indicate that the amount of lymphoid tissue is greater than it was at some previous time, but the lymphoid nodes are still few and far apart. No evidences of Hassell's corpuscles are found.

Other Viscera. In the *kidney* are numerous accumulations of lymphoid tissue, the largest not over 0.5 mm. in diameter, and located only in the cortex in the sections examined. These cells are of the lymphoid type almost exclusively; are arranged in illy defined groups, infiltrating between the renal tubules which seem to be destroyed when surrounded by the cells. Plasma cells and eosinophiles are absent from these areas. The *liver* is studded with lymphoid areas, which follow along the course of Glisson's capsule at all points; it is impossible to find a group of the vessels not surrounded by the new cells. The largest of these areas is the size of a liver lobule. No such areas are found in any part of the lobule except about the portal vessels. The cell masses do not tend to infiltrate between the liver columns as they do between the renal tubules, but rather push them aside *en masse*, for which reason, probably, the new cells are often elongated and irregular. Plasma cells and eosinophile cells are not found. In the *prostate* are many accumulations of lymphoid tissue, some 1 to 2 mm. in diameter, infiltrating extensively between the muscle fibres. There are some small accumulations in the *adrenal*, chiefly in the medulla about the large vessels, and a few are found about the vessels in the interstitial tissue of the *pancreas*. The *thyroid*, *testicle*, and, so far as examined, the *lungs* were free from lymphoid proliferation.

The Blood. As no examination had been made during life, smears were made from the heart's blood at autopsy, but for some

reason it was impossible to secure satisfactory stained preparations from these. It could merely be determined that there was no apparent increase in the number of leukocytes, and that of these more than the usual proportion were lymphocytes. Examination of the blood in the sections of the various organs made it seem that there was little more than the normal number of leukocytes in the blood. An attempt at a differential count was made by counting the leukocytes in the larger vessels in the capsule of the thyroid and the testicle in several sections; these organs were selected as offering less possibility of "dragging in" of cells by the knife, and as being most nearly normal of any of the organs. Vessels with thrombi or unusual collections of leukocytes were excluded. Only cells that were definitely either lymphocytes or polymorphonuclear leukocytes were counted, transitional and doubtful forms being excluded, and of 500 cells so counted 47 per cent. were polymorphonuclear and 53 per cent. lymphocytes. It must be borne in mind that death in this case was due to suppurative peritonitis, with terminal septicæmia.

Bacteriological Examination. Staphylococcus pyogenes aureus was obtained from the heart's blood and viscera, and was associated with B. coli in the peritoneal exudate.

Animal Inoculation. Five guinea-pigs were inoculated with 2 cm. each of thick emulsion of glands, taken from all parts of the body and ground up together. The pigs were inoculated intraperitoneally on November 17th. One died after four days with an acute pneumonic process. No peritoneal or other changes. One died on December 14th with a pneumonic condition, and showed no evidence of tuberculosis. However, one peripancreatic gland was 15 mm. in diameter, and contained a large amount of very thin pus, forming little more than a sac for the pus. This pus was stained for tubercle bacilli with negative results; likewise the wall of the abscess. Histologically it seemed a simple pus sac. After two months the three surviving guinea-pigs were killed, and found perfectly normal; no evidence of the injections of any kind; no tuberculosis, no lymph-gland enlargement.

ANALYSIS. In all but one of these eight cases, including our own, the ages varied between forty and sixty, the average being a little over fifty. Murchison's case, which is included by some of the English writers, is almost certainly lymphosarcoma, and not pseudoleukæmia in the ordinary sense. Schlesinger's series of lymphosarcoma of the stomach shows the most frequent age of this closely allied condition as between twenty and thirty-five. There were six men and two women, which agrees with the greater frequency of pseudoleukæmia in men.

In every case there was greater or less general enlargement of the lymph glands throughout the body. In some the greatest increase was in the cervical glands; in others, especially in our case, in the

abdominal glands receiving the lymph from the involved portions of the alimentary tract.

Enlargement of the spleen is nearly constant, in the largest the weight being forty-four ounces. More characteristic is the constant enlargement of the Malpighian bodies, which was marked in all. The liver is less frequently enlarged, but in some of the cases is the seat of considerable lymphoid infiltration and enlargement, as in our case. The kidneys seem to be less often affected than the liver. In other words, the distribution of changes outside the gastrointestinal tract is not different from what may be found in any ordinary cases of pseudoleukæmia.

As for the alimentary tract itself, it is observed that the form taken by the hyperplasia varies somewhat with the location. 1. Immense, loose, sinuous folds, like cerebral convolutions, are found in the stomach. 2. Polypoid forms, those of pea-size almost countless in number, increasing to the size of chestnuts. 3. Extensive slightly raised patches corresponding to Peyer's patches. 4. These polypoid growths and patches are frequently pigmented a slaty black, and less frequently ulcerated. Outside of the infiltrations the mucous surface is usually normal, and the ulcerations are usually slight and superficial. The tissue increase is limited to the mucous and submucous coats, the muscularis not being invaded to any extent. An interesting fact is that in spite of the enormous thickenings the lumen of the bowel is not altered in size.

Stomach. In every case but one the mucous membrane of the stomach was thrown into great sinuous folds, ulcerated to a slight extent in three cases, but maintaining usually its normal external appearance. The immediate vicinity of the pylorus was not involved in some of the cases. Pitt remarks that it is not clear why the growth is so scanty at the pyloric end of the stomach, where, according to Watney, the lymphoid tissue is so abundant. The duodenum is least affected, having very few or no lesions.

The small intestine in every case presented small, pea-sized polypoid growths, and extensive pigmented, flat infiltrations of Peyer's patches. In the region of the ileocæcal valve and appendix the thickening in every case was enormous. Next to the duodenum the large intestine was least affected.

The clinical symptoms were very meagrely reported in most of the cases. They present the usual conditions of pseudoleukæmia, with rarely any symptoms to indicate that the gastrointestinal tract was involved, probably because there is no obstruction to the bowel and no ulceration of the surfaces. Stoerk's patient showed bloody stools, and in our case the history of digestive disturbances and the palpable tumor led to an exploratory laparotomy.

General Summary. The frequency with which the first or most extensive enlargement of the lymph glands in Hodgkin's disease has been observed in the cervical region has suggested to many the

possibility that the infectious agent, if such there be, might have entered *via* the tonsils, infected the cervical glands, and later become generalized throughout the body. Such a conception is supported by the cases of pseudoleukæmia discussed here, and particularly by the one we report. In this instance by far the most advanced manifestation of the disease was in the stomach, and next to the stomach the glands that receive its drainage. Although all the lymph glands were more or less enlarged, none compared with those about the stomach in size.) Another peculiarity noted, in reviewing over two hundred autopsies in pseudoleukæmia as recorded in the literature, was that whereas in the universal enlargement of lymphatic tissue that of the alimentary canal usually participates little or not at all, yet when it does become involved to any extent it is likely to happen that it is then involved much more in proportion than any of the other lymphatic tissues. This recalls a similar peculiarity of many known infections, *i. e.*, that when they once have made headway with a certain sort of tissue they often tend to invade almost exclusively similar tissues in other parts of the body. This tendency to affect the gastrointestinal lymph apparatus, as seen in this particular group of cases of pseudoleukæmia, has seemed to warrant their collection and publication together as a subdivision of the general group of cases that presents the anatomical and symptom-complex of Hodgkin's disease, to call attention to their existence. Apparently this group in which the chief alterations are in the gastrointestinal tract is neither clinically nor etiologically different from the ordinary cases, and anatomically the difference lies solely in the distribution of the lesions.

Such cases stand particularly near the lymphosarcomas, and the confusion in nomenclature of pseudoleukæmia has added to the difficulty of distinction in many of the recorded cases. Murchison's case, according to his description, is an example of a real malignant tumor, a lymphosarcoma of the duodenum with involvement of the regional glands, yet it has been classified in the literature as pseudoleukæmia. Limiting the term lymphosarcoma to true malignant tumors, there can be no question of sarcoma in the cases we have under discussion, for they do not infiltrate, they attack only lymphoid tissue, and in doing so disobey all the laws of metastasis, and they possess particular histological features that are incompatible with sarcoma. Following up the changes in the lymph glands in our case in the order of extent of enlargement, it is readily determined that the growth is derived from the cells of the glands themselves, which multiply from certain anatomical locations in the glands, and pass through certain steps in their development, and that it is not a matter of growth from foci of cells entering the gland from without and assuming a certain fixed type, as would be the case with a metastatic growth. The best proof of all, perhaps, is the readiness with which the cases of lymphosarcoma of the

digestive tract can be separated from these forms of pseudoleukæmia by the anatomical findings reported, no matter under which of several names they may be found classified.

Tuberculosis as a cause of Hodgkin's disease has been thoroughly discussed of late with a negative verdict, although certain cases show that we may have clinically a symptom-complex not different from that of Hodgkin's disease, associated with universal tuberculous lymphadenitis. Our case may be added to the now fairly considerable number in which animal inoculation as well as microscopic examination has failed to demonstrate the presence of tubercle bacilli.

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THREE RECENT CASES OF CROUP DUE TO STAPHYLOCOCCUS AND REQUIRING TRACHEOTOMY.[1]

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CROUP is a term which has by time and usage earned a permanent position in our medical vocabulary, and yet with the progressive development in modern pathology its meaning grows steadily more ambiguous. Heretofore such prefixes as "true," "pseudo," "membranous," etc., helped to designate the special form intended; for example, membranous croup meant laryngeotracheal diphtheria due to the Klebs-Loeffler bacillus. Billings in a bacteriological analysis of 286 cases of membranous laryngitis showed 80 per cent. to be due the Klebs-Loeffler bacillus and 20 per cent. to streptococci and diplococci. We also know that pseudomembranes may be induced by the local action of chemical and physical agents. Gould's dictionary defines "croup" as "a disease of the larynx and trachea of children, prominent symptoms of which are peculiar cough and difficulty in breathing; it is often accompanied by the development of a pseudomembranous deposit or exudate upon the parts." The latest authorities still differ as to the proper interpretation of various

[1] Read at the Cleveland Meeting of the Ohio State Medical Association, May 20, 1904.

prefixes placed before the term croup. Jonathan Wright, in his latest text on nose and throat diseases gives a special heading entitled "Acute Catarrhal Laryngitis in Children"; this title will best include the cases to be described in this paper. The clinical characteristics of acute laryngitis are familiar to every medical practitioner, and I shall proceed at once with three interesting cases which came under my observation last winter.

CASE I.—A male babe, aged eleven months, was of fair build, and had always been well. On December 1st the mother had "aching in the bones," a chill, fever, sore throat, and enlargement of the cervical glands. The next day the older of her two children, aged three, took sick with the same symptoms. On the third day the babe was similarly affected, and drowsiness was especially noted. The mother was well in about ten days, but the children continued in their ailment, some days better, then again worse. After domestic remedies had been used for about two weeks, Dr. Vance was called, who pronounced the condition tonsillitis. He found the temperature ranging from 101° to 102°, and on several visits the same was normal. At the end of the third week the babe became "croupy," and the glandular swelling on the right side of the neck became larger and more diffuse, simulating a cellulitis. The next day the breathing was more labored and with a distinct stridor audible all over the room. The following night strangling spells caused much anxiety. The following morning the symptoms subsided, but the breathing was still labored. At noon I was called to make a bacteriological examination of the throat. I found moderate hyperæmia and swelling of the pharynx, but no membrane. The throat swabs showed microscopically the presence of a few saprophytic bacilli and a predominance of diplococci. Late in the afternoon the child had a temperature of 103°, weak and rapid pulse, pallor and cyanosis, and beginning coma. Tracheotomy had been advised the day before, but was refused. Consent now being given, the chances even with operation were very doubtful. Dr. Rind did a "high operation," and on opening the trachea nothing more than a slight congestion with small quantity of mucus exudate was seen. Swabbings taken from both larynx and trachea showed on subsequent examination pure cultures of a diplococcus. Probing toward the larynx, this was found occluded by intense swelling. Respiration gradually became rhythmic, and thirty minutes later the child was placed in bed quietly breathing through the tube. The color and pulse improved rapidly. From this time on a tabulated record was kept which showed for the following few days a temperature ranging from 101° to 104°; pulse, 135 to 140; respiration, 40 to 50. The cellulitis on the right side of the neck subsided within the next two days, but the swelling in the larynx continued for five days, whereupon the breathing was re-established through the natural channel, and the tube was left out alto-

gether. Strict asepsis was observed throughout, but considerable suppuration occurred in the wound, due, probably, to the organism found in the trachea. The wound healed by granulation in two weeks. The child made a perfect recovery, and is well to-day. In passing it may be mentioned that the nurse who waited on the mother during her illness was taken with sore throat and glandular enlargement the week following her departure; moreover, the daughter of the nurse was similarly affected.

CASE II.—A female, aged four years, quite plump, had always been well excepting throat trouble during the winter months. About four weeks before the present trouble the whole family, including father, mother, and two children, had mild sore throats. Dr. Rind was called several times to see patient aged four, because she seemed to be worse than the others. He found nothing significant, and made a diagnosis of tonsillitis. On January 7, about three weeks from the onset, the patient had "croup" symptoms. Dr. Rind being ill, Dr. Vance was called, who found a temperature of 101°, pulse 130, high falsetto voice, and respiratory stridor. On the same day I was called to make a throat examination and found moderate congestion and swelling of the larynx, but no membrane. The throat swabs showed a few non-characteristic bacilli and a predominance of diplococci. It was evident from close clinical observation that the obstruction was both mechanical and spasmodic. During the afternoon the condition grew progressively worse, and 5000 units of antitoxin (Mulford's) was given as an extra precaution. About two hours after this the child had its worst strangling spell, and the nurse thought it was dead. I arrived fifteen minutes later and found the child recovered from the attack, but in general the condition was worse than before. In the evening four physicians in consultation decided that operation should be done. The temperature was now 102°, and pulse 130. At 9 P.M. Dr. Rind opened the trachea high up, which was difficult, owing to the excessive adipose tissue and engorged veins. When the trachea was incised no air entered, and we feared membrane. However, on closer inspection a diaphragm was visible, extending obliquely across the lumen of the trachea, and on puncturing this air entered with a gush. This diaphragm must have been either an anomalous structure or an old organized membrane, for it was quite firm, deep pink, and not unlike the surrounding mucosa; Moreover, no other evidence of pseudomembrane was found. The larynx was impervious on probing.

Smears taken from the mucosa showed diplococci in a pure state. A small quantity of frothy mucus was blown up through the tube from the bronchi. The child was placed in bed breathing perfectly and with good color and pulse.

About one hour after operation the temperature was 103°; pulse, 130; respiration, 30. Stimulants were given freely. Next

morning at 3 o'clock the heart began to fail, and this continued until the following afternoon, when the child died, apparently from profound toxæmia. Just before death the temperature was 107° (per rectum); pulse, 150, and respiration, 50. At this time my incubator cultures developed sufficiently to show the absence of bacilli. The clinical phenomena were so unusual and suspicious that my bacteriologic findings were accepted, but not without some hesitation.

Case III.—A male babe, aged five years; had measles at the age of two years, but was otherwise well. The tonsils were chronically enlarged, and each winter he would have sore throat and "croup." On January 28th the child had one of its familiar attacks of sore throat, and three days later the voice was hoarse and the cough "croupy." During the night he had several choking spells. Next morning Dr. Seward was called, and he found the tonsils filling the throat, but no membrane. The symptoms at the time of his visit had subsided. In the afternoon drowsiness occurred, and all night the child struggled for air. Next morning Dr. Rind was called into consultation, and at this time the condition was so grave that he hastened for his instruments and assistants. I was called to make a throat examination. The patient was already on the table with the trachea opened. I took my culture smears through the wound and from the mucus blown out from the tube. Microscopically, the smears showed only diplococci, which were numerous. The mucosa appeared congested and the larynx was swollen shut, but no membrane was found. I was told that the child was blue and comatose before operation, and no anæsthetic was required. Antitoxin (5000 units) were given at the time of the operation. The breathing and color improved after the tube was in the trachea, but the pulse remained weak, and the child died about two hours after operation. At my request Dr. Vance procured a section of the larynx, the findings of which I shall report farther on in this paper.

Cases I. and II. lived in the same block; Case III. lived eight squares from the other two, and no evidence could be secured, making it probable that a contagion was carried from one to the other or from outside sources. It may also be stated that the three cases occurred in families in comfortable circumstances, and the hygienic environment was good.

The bacteriologic investigation of these cases involved about four months of research, a complete report of which would be impractical in this paper. I shall merely give a synopsis of this work.

Unfortunately, in Case I. the cultures were destroyed after a few days' growth. However, the essential characteristics of the organism, both microscopically and culturally, together with the extensive suppuration induced, leads me to believe that it was similar

to that found in Cases II. and III. In the last two instances the cultures were carefully grown in both incubator and room temperature. The findings in Case II. were as follows:

On moist streak agar pinpoint colonies were visible after twelve hours' growth in the incubator at 37° C. The mature colonies consisted of a slightly elevated slimy mass, with smooth wavy border, and varying in color from milky white to canary yellow. The color characteristic of the colony was often lost in transplanting. Blood serum tubes showed almost the same appearances.

In bouillon, rapid clouding with subsequent deposits of granular pigment was produced. Stab cultures in gelatin showed finger-shaped liquefaction with pigmented deposit in the pendent part. Gelatin plates contained pin-point grayish colonies which soon enlarged, giving rise to saucer-shaped depressions and final liquefaction of the medium. In litmus milk slow coagulation and acid formation occurred; the casein was subsequently liquefied. The cultural tests in Case III. were almost identical, excepting the pigment variation was less marked. Besides this a few of the original cultures were contaminated, owing probably to the fact that the field of operation could not be properly prepared, and dispatch was certainly paramount in this instance.

Microscopic examination of these cases proved the organism to be a coccus occurring single, more often in pairs, and frequently in clusters. The individual organism varied in size, which was especially noted in those composing the short chains found in the liquid media. The cocci stained both by simple aniline dyes and also by Gram's method. Variation in the intensity of staining was observed in many instances.

From the above observations I was assured that the organism was the staphylococcus. The irregular behavior of the pigment formation led me to omit any conclusion as to the prevailing type of staphylococcus involved.

Coincident with the cultural work the pathogenesis was determined by inoculating white mice. In Case I., as stated before, the cultures were destroyed. In Case II. the staphylococcus grown on blood serum for three days in the incubator (37° C.) was transferred to bouillon, and after twelve hours' growth was injected subcutaneously near the root of the tail in two mice. One received 5 drops and died within sixteen hours; the other received 10 drops and died eleven hours after inoculation.

Post-mortem examination of the mice showed slight changes, consisting mainly of congestion and moderate œdema of the tissues. Smears and cultures taken subcutaneously, intraperitoneally, and from the blood showed cocci in large numbers. Microscopic sections of the organs showed small numbers of the same organism. The peritoneal smears revealed marked leukocytosis, and many phagocytes loaded with cocci were witnessed with much interest.

The pathogenesis having been in a measure ascertained, I next attempted to determine the degree of virulence and probable means of accidental infection. Healthy mice placed in the infected cages remained well. Contamination of the food and drink with fresh cultures proved negative. After five weeks of incubator growth the organism in culture was again inoculated subcutaneously into healthy mice, using fresh bouillon cultures, but these failed to kill even in large doses. Abscesses, however, formed at the point of inoculation. Cultures attenuated by three months' growth in the incubator were next injected into the peritoneal cavity of white mice. They recovered from the inoculation of 5 drops of fresh bouillon culture, but 15 drops killed within twenty-four hours, and on post-mortem examination overwhelming numbers of staphylococci were demonstrated by smears, cultures, and sectioning of the organs.

Cultures from Case III. were similarly tested, and practically the same results were obtained. Larger doses for intraperitoneal injection were necessary to kill, which was either due to lesser virulence of the organism or more rapid attenuation by artificial growth.

The section of trachea removed from Case III. was sectioned and stained. Microscopically it showed small cell infiltration of the mucosa, submucosa, and muscularis. The mucosa had a few superficial erosions upon which were deposited masses of cocci. There was no evidence of fibrin or pseudomembrane. Staphylococci in small numbers were also found in the interstitial stroma of the submucosa and striped muscle bundles.

To briefly summarize the essential points, we have here three cases of preliminary sore throat in children, followed by severe obstructive symptoms in the larynx, and requiring tracheotomy. In none of the cases was there evidence of a pseudomembrane. The clinical symptoms pointed to a local infectious process with elaboration of toxins. In two of the cases the diagnosis of diphtheria was entertained, and antitoxin was given, but with negative results. Bacteriological examination revealed the presence of practically pure cultures of staphylococci in the trachea and larynx. The organism in recent artificial cultures proved to be unusually pathogenic to white mice. Subsequent inoculation of the same strain of bacteria proved much less virulent. Pathogenesis was displayed only by direct inoculation into the lymph or blood circulation.

From an analysis of this investigation we may safely draw the following conclusions:

1. The winter epidemics of tonsillitis and sore throat in children at times give rise to laryngeal complications.

2. This condition is always serious owing to the ease with which the juvenile throat may be obstructed.

3. Individual predisposition to laryngeal complication is quite probable.

4. The staphylococcus, a common denizen of the throat, may, under favorable conditions, give rise to grave symptoms, as exemplified in the above cases.

5. The rapidity of onset and severity of symptoms may at times suggest diphtheria.

6. A reliable bacteriologic examination of the throat is a prerequisite.

7. Antitoxin, although to be used in doubtful cases, will be of no service in cases in which the Klebs-Loeffler organism is not the causative factor.

8. The above may be taken as examples of cases at times diagnosed as diphtheria in which no microscopic examination is made. Moreover, the failures of antitoxin are often credited to such cases.

9. Finally, I would emphasize the importance of a careful analysis of each case, basing the diagnosis on both clinical and bacteriologic evidence.

A STUDY OF THE GROUP ACTINOMYCES.

WITH THE REPORT OF A PATHOGENIC SPECIES FOR MAN.

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Historical Review. Before describing the organism which was isolated from an abscess of the lung, I shall review some of the important points concerning the group actinomyces and its increasing importance in pathology.

In 1875 F. Cohn[1] described an organism which Foerster had found in the human lacrymal canal. This he described as a filamentous growth which showed true branching forms. Despite this description the organism and others resembling it were confused with cladothrix by a number of different authors. Even such men as Baumgarten[2] and Nocard[3] placed actinomyces and streptothrix du farcin du bœuf in the genus cladothrix. The demonstration of actinomyces by Nocard as the cause of a disease in animals soon caused investigators to study it more closely, and it was soon separated from cladothrix, since the false branching of this organism sufficed to distinguish it from a streptothrix with true dichotomous branching.

The streptothrix* since this time has been found in a large number of pathological and saprophytic conditions.

* The name streptothrix is used in an historical sense, but the name actinomyces is later given to the entire group.

Almquist[4] isolated one species from a case of meningitis, and found another variety in water, which gave a white growth. Gasperini[5] obtained streptothrix Foersteri from the air, and found a second species which was negative when inoculated into guinea-pigs and rabbits. This was chromogenic, forming a brown color.

The observations of Eppinger[6] are of special interest.

He observed a streptothrix in a case of meningitis and cervical abscess, which caused pseudotubercles when injected into the tissues of guinea-pigs and rabbits. The branching threads stained by Gram's method, and formed coccus-like spores. Gruber[7] also found one of these organisms which produced abscesses in guinea-pigs, and Doria[8] by exposing gelatin plates to the air cultivated thirty-five colonies of streptothrix alba of Gasperini, and seven colonies of streptothrix nigra. The four other chromogenic species were whitish-yellow, pink, orange, and violet. These species all seemed similar under the microscope, and formed spores. Sauvageau[9] also found two specimens of a streptothrix in gelatin plates exposed to the air.

Bollinger and Harz[10] first called the fungi found in actinomycosis by the name of actinomyces. Following this observation a large number of articles appeared on this subject. Boström[11] has studied and carefully described one form of streptothrix actinomycotica which is aërobic, and pathogenic for man and cattle, and not pathogenic for laboratory animals, such as guinea-pigs and rabbits. Wolf and Israel[12] soon described another species which differed from the former in growing best under anaërobic conditions, and in being pathogenic for small laboratory animals. They obtained it from two cases in human beings. Levy[13] found an anaërobic species in five cases of human actinomycosis, and Asthoff[21] isolated this species from a case of primary actinomycosis of the lung.

Streptothrix has been observed quite recently in a number of diseased conditions in animals and human beings.

Silberschmidt[14] found an organism in the lungs of a goat with a disease resembling tuberculosis. He called it streptothrix capræ. This species consisted of filaments staining by Gram's method, which grew on all the culture materials and produced abscesses or pseudotubercles in guinea-pigs and rabbits.

Aoyama and Miyamoto[15] described a form of streptothrix which they cultivated from the pus from a lung affected with caseous pneumonia and purulent pleuritis. The organism was present during life in the sputum. It proved as resistant to acids as the tubercle bacillus, but grew readily as a streptothrix on the various media, and produced pseudotubercles and fibrinohemorrhagic exudations in animals.

Two cases of necrotic bronchopneumonia have been recently reported by Norris and Larkin[16] as caused by a streptothrix. Both patients suffered from clinical conditions resembling lobar pneu-

monia, and at the autopsies the lungs showed complete consolidation, and one case also exhibited a fibrinous pleuritis. The lungs in both cases, upon histological examination, showed a necrotic or purulent bronchitis and purulent exudation in the alveoli with small diffuse abscesses. A few threads of the streptothrix were found in the air cells, but the necrotic bronchi contained many colonies of the streptothrix. The lung also contained many streptococci. These organisms were stained by Weigert's method.

Some difficulty was experienced in separating the streptococci from the streptothrix, but by cultivating the material from infected rabbits on sterile normal kidneys, and then transferring the colonies to broth, a pure culture was at last obtained.

This then grew on the usual culture materials, although it had first refused to do so. The injection of the streptococcus and the streptothrix together into rabbits produced suppurative and necrotic pneumonia and bronchitis, but when pure cultures of the streptothrix were injected into the tissues death did not often occur. These injections, however, caused abscesses, and pseudotubercles, and the organism can be considered as pathogenic.

Fullerton[17] found a pathogenic streptothrix in the case of a woman, aged forty-six years, who had suffered from a cough for twelve years. On admission to the hospital the patient had bloody expectoration and pulmonary rales, and an abscess in the left axilla and over the clavicle. The streptothrix was found in the sputum, and a pure culture showing mycelium and spores was obtained from the pus. It grew on glycerin-agar and broth, and was not pathogenic for rabbits. Scheele and Petruschky[18] also report a case of pulmonary infection due to this organism. The woman suffered from fever, thoracic pain, and pulmonary symptoms. Small tumors filled with pus appeared at different points under the skin. The streptothrix was found in the sputum and pus during life, and an ante-mortem diagnosis of streptothrix infection was made. At the autopsy the streptothrix was found in the solidified lung, and the metastatic abscesses. It grew on gelatin, and in bouillon.

In the chronic inflammatory process usually affecting the tissues of the foot called mycetoma, or Madura foot, a form of streptothrix has been isolated from one variety of cases. In the pus from the ochroid, or pale variety of the disease, granules have been obtained which grow on potato as a typical streptothrix. Vincent[23] and Boyce and Adams[19] have all probably cultivated a form of streptothrix from such cases, which belongs to a different species of the genus streptothrix from that of actinomyces bovis.

Sabrazès and Rivière[22] isolated a form of actinomyces from a case of abscess of the brain, lungs, and kidney. This organism stained by Gram's method, showed irregularity in staining, and true dichotomous branching. Its mixture with other bacteria

prevented its further study. Berestneff, in a Russian publication quoted by Hektoen, also reported a specimen of actinomyces asteroides which he isolated from an abscess of the brain.

It will be noted that thus far I have used the names which have been applied in a rather confusing way to the various species of this group. Hektoen[24] and later MacCallum[20] have pointed out that priority is alone valid in determining nomenclature, and after weeding out the various other names for this genus they correctly conclude that actinomyces must be used for all the species of this group. These organisms in the future will, therefore, be called actinomyces.

MacCallum also isolated a specimen of actinomyces asteroides from a case of general subacute purulent peritonitis in a child aged three years. This condition followed a gastrostomy for the relief of an œsophageal stricture. As this organism will be minutely described in the section on classification, no further comment will be made at this time.

Description of Case and Organism. The organism which I shall describe was obtained in pure culture from an abscess of the left lung in a case of marasmus in the service of Dr. John Ruhräh at the Garrett Hospital.

Clinical History. The child was a white male, aged twenty-eight days. The temperature showed no elevation, and the child died at last from wasting and exhaustion. Cyanosis was present, the spleen was palpable, and a few rales were detected in the lungs.

Record of Autopsy. The body weighed four pounds, and the cervical glands were enlarged. The subcutaneous and subperitoneal fat was light yellow and of a granular appearance. The thymus gland only weighed 2.1 grams, and measured 3.5 by 2 cm., being 6 mm. in thickness. This organ, therefore, showed the atrophy characteristic of marasmus.

The lower portion of the lower lobe of the left lung at the middle part of its diaphragmatic surface showed a small projecting area, which, on section, proved to be a pus cavity about the size of a pea. All of the other viscera were normal in appearance.

A culture from the abscess on blood serum gave a pure growth of the actinomyces to be described farther on.

Histopathology. *Lung Abscess.* The lung tissue surrounding the abscess is deeply congested, and the air cells are filled with an exudate consisting of red blood corpuscles and endothelial cells. The abscess itself simply consists of a collection of polymorphonuclear leukocytes, containing many branching threads staining by Weigert's method.

Lung. Left lung. The smaller bronchi are filled with an exudate consisting of polymorphonuclear leukocytes, red blood corpuscles, and cells with round nuclei surrounded by eosin-staining protoplasm. The lung tissue surrounding these bronchi has under-

gone great thickening, and is richly infiltrated with young connective-tissue cells with round, oval, or elongated nuclei. Many of the interalveolar septa are greatly thickened, and some of the air cells and infundibula adjacent to the inflamed bronchi are filled with pus cells. There is also marked congestion of the interalveolar capillaries. On staining sections by Weigert's method a firm network of branching threads is to be seen in the abscess. No coccus-like bodies or clubbed ends are present, and the growth consists entirely of threads.

Thymus Gland. Fibrous capsule somewhat thickened. The interlobular tissue is markedly thickened, cutting up the lobules into irregular masses. Some of these irregular lobules contain as many as fifty degenerated Hassall's bodies. These bodies are dilated, and they usually contain a central body composed of concentrically arranged hyaline material. Between this and the lumen there is usually a peripheral rim of polymorphonuclear leukocytes, although sometimes this rim is simply a clear space. This rim is surrounded by a single layer of flat cells resembling endothelium. There also seems to be an increase of reticular tissue and reticular endothelium within the lobules, and the lymphocytes are not as numerous as those in the normal gland. Sections were made from all of the other viscera, but no abnormal changes were found. Cultures from the viscera remained sterile. The macroscopic and microscopic changes, therefore, simply indicated a case of marasmus in which the terminal infection was caused by a species of actinomyces.

DESCRIPTION OF THE ORGANISM. The serum tube, which was inoculated from the pus from the lung, did not show any growth for six days, and at the end of this time a number of fine, white, pinpoint dots appeared on the surface of the medium.

Morphology. In fresh specimens the colonies consist of branching threads about twice the transverse diameter of a typhoid bacillus. In the meshes of these threads and at the distal ends there are a number of round bodies free in the fluid.

When the colonies are teased out or gently crushed they can be mounted on a slide and stained by Gram's method. The threads are long and often show side branches. The staining is interrupted or irregular, areas of dark-blue protoplasm alternating with unstained areas of protoplasm. The spores are often grouped around the distal end of a thread, and are about twice the size of an ordinary micrococcus. There are also smaller round spores free in the field, often arranged in chains resembling streptococci.

Spores. When a colony is stained by the Ziehl-Gabbett method the numerous ovoid spores retain the red dye. Some of these spores almost resemble bacilli, although they are not as long and thin as the tubercle bacillus. Most of the hyphæ or threads of the colonies stain blue, showing no resistance to acids. A few, however, stain bright red, and these sometimes seem to cut off their ends by trans-

verse fission and form spores. These are the special hyphæ mentioned by Poncet and Berard in their book on *Actinomycosis*, which form the spores, while the ordinary mycelium does not form any spores. On staining with carbol-fuchsin the irregular, almost striped staining is well seen, but Loeffler's and Neisser's stains show no metachromatic bodies. This result differs from that obtained by MacCallum, who obtained many bluish-black metachromatic granules. He did not obtain any spores, but our results with the Ziehl-Gabbett stain certainly indicate the formation of spores. The threads in hanging drops are not motile.

CULTURAL CHARACTERISTICS. 1. *Blood Serum.* The colonies form small, elevated, round, adherent dots of a golden-yellow color. The medium is not liquefied.

2. *Slant-agar.* The colonies are simply small white adherent dots which later coalesce into a yellow membrane.

3. *Sugar-agar.* The organism grows as a number of fine, elevated, brownish-yellow dots along the track of the needle.

4. *Potato.* The colonies appear as fine dots which later form a yellow spreading membrane. The growth is very adherent.

5. *Milk.* This medium becomes covered in one week with a thick yellow membrane, with elevations and depressions resembling a relief map. Litmus milk is rendered alkaline.

6. *Gelatin.* Not liquefied. Colonies are fine, white, adherent dots.

7. *Dunham's Solution.* A slight growth takes place in about five days, but no indol is formed even after two weeks.

8. *Nitrate Solution.* After two weeks' growth in the nitrate solution a few colonies are present, and a slight nitrite reaction takes place.

FERMENTATION TUBE. The organism does not cause gas formation in glucose, lactose, and saccharose bouillon, and does not grow in the closed branch of the fermentation tube.

In glucose bouillon in a flask the growth is very luxuriant, and in one week a white membrane forms on the surface of the bouillon. This later becomes wrinkled, and at the end of a month the surface growth has formed a number of round, knob-like elevations, varying in size from that of a pinpoint to a diameter of 3 mm. Some of these knobs are white, some are a dull golden-yellow, and a few show a combination of both of these colors. The colonies seem to need but little nourishment, as they even develop on the sides of the glass which has been moistened by the bouillon.

The development in glucose bouillon in the fermentation tube or flask might be considered as characteristic.

ANIMAL EXPERIMENTS. A suspension of 2 c.c. of the organism from serum was injected into the abdominal cavity of a guinea-pig, and the animal died in four days. The slight exudate consisted of small lymphocytes, large lymphocytes, polymorphonuclear leukocytes, red blood corpuscles, and endothelial cells. The liver con-

tained a few dots resembling tubercles. Cultures from the liver and peritoneal exudate gave a pure culture of actinomyces.

A rabbit was also given 3 c.c. of a bouillon culture of one week's growth. The injection was made in the peritoneal cavity. The animal died in one week, and only a few yellow nodules containing actinomycetes were found scattered over the peritoneum. One white rat injected subcutaneously in the abdominal wall with 3 c.c. died in ten days. There was a small caseous area at the seat of injection, and the organism was isolated from this area, but the viscera were sterile.

Another guinea-pig received 2 c.c. in the abdominal cavity, and the animal died in twelve days. The report on the autopsy is as follows:

Guinea-pig; 3 c.c. of bouillon injected in abdominal cavity on February 25th. Died on March 9th.

Body emaciated. Inguinal glands enlarged. The abdominal cavity was free from any exudate, and quite dry. In various places to be mentioned below, there were solitary, gray, firm masses about the size of a tubercle, which always projected from the peritoneal surface. These pseudotubercles were found on the upper surface of the liver, on the parietal peritoneum, in the shrunken great omentum, on the surface of the bladder, the gall-bladder, broad ligament of liver, posterior abdominal surface of lower sternum, and the diaphragm. Only from one to three pseudotubercles were found in each of these situations.

The thoracic organs and the other viscera seemed normal.

Cultures were taken from the abdominal cavity and the liver, and actinomyces was recovered.

The last guinea-pig received an injection of 2 c.c. directly into the pleural cavity, and the animal lived seven days. The result follows:

Thoracic Cavity. The chest wall is deformed; the sternum, instead of being in the median line, is curved somewhat in the shape of an S, and has been thrust into the right mammary line. The anteroposterior line between the midsternum and the dorsal vertebræ is deflected to the right at an angle of 45 degrees.

The left pleural cavity contains some fibrinous adhesions binding the chest wall to the lung. The right pleural cavity in its posterior portion contains 10 c.c. of a thick bloody fluid. The entire dorsal curve of the vertebræ is deflected to the left, having lost most of its anteroposterior curve. The entire parietal and diaphragmatic pleura on both sides, especially in the intercostal spaces, contains numerous gray, pinpoint areas resembling tubercles.

Lungs. Both lungs are compressed, and their surfaces are covered in places with thick patches of yellow membrane. This fibrinous inflammation has also invaded the mediastinum as thick conglomerate pseudotubercles, and these grayish dots can also be made out on the parietal layers.

Lung Tissue. The lung on cut section is congested and contains many grayish, pinpoint pseudotubercles; the right lung presents a similar appearance.

Abdominal Viscera. The abdominal viscera are normal, with the exception of the liver; this contains a few yellow areas which look simply like distended vessels.

Microscopic Examination. One of the pseudotubercles from the mediastinum on being teased out consists principally of cells with large, round nuclei surrounded by granular protoplasm often containing fat-drops. There are also small lymphoid cells, and few kite-shaped or spindle cells. Here and there can be made out typical branching threads stained by Gram's method.

Gall-bladder. Gall-bladder contains many red blood corpuscles.

The cultures from the heart, kidney, and liver and lung tissue are sterile on blood serum and agar. The cultures from the pericardial cavity and both pleural cavities on blood serum and agar contain numerous typical colonies of actinomyces. The colonies on serum are of a golden-yellow color. These colonies, examined under the microscope, are typical examples of actinomyces, staining by Gram's method. It will be seen that this organism when injected into animals caused local nodules, either on serous surfaces or in viscera, which had a tendency to undergo necrosis.

Description of the Microscopic Changes Produced in Human Beings and Experimental Animals. In the cases reported by Eppinger, MacCallum, and myself the lesions in human beings simply consisted in a purulent exudation respectively in the brain and meningeal cavity, in the peritoneal cavity, and in the air cells of the lung. Aoyama and Miyamoto found fibrinopurulent pleurisy and an abscess of the right lung.

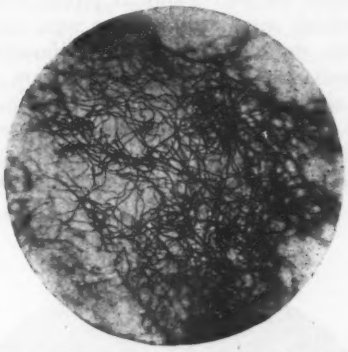
When the organism was injected subcutaneously in animals an abscess usually resulted, but when introduced into the general circulation or into any of the serous cavities a large number of small granulomata or so-called pseudotubercles were produced. These lesions thus differ from those described in human beings.

MacCallum has made a very careful study of the histogenesis of these lesions by studying the early changes in animals (in two rabbits) killed four and six hours after inoculation. The capillaries of the lungs were crowded with leukocytes. This was the first response to the presence of actinomyces asteroides. The lung of an animal killed twenty-four hours after inoculation already contained small nodules consisting of widely distended bloodvessels surrounded by alveoli, and their lumina were richly infiltrated with leukocytes. These nodules later undergo extensive necrosis, which process is the later result of the presence of the organism. These nodules never coalesce into larger distinct abscesses or cavities.

I was not able to confirm the early lesions described above, since I only examined animals that died at a much later period; but in

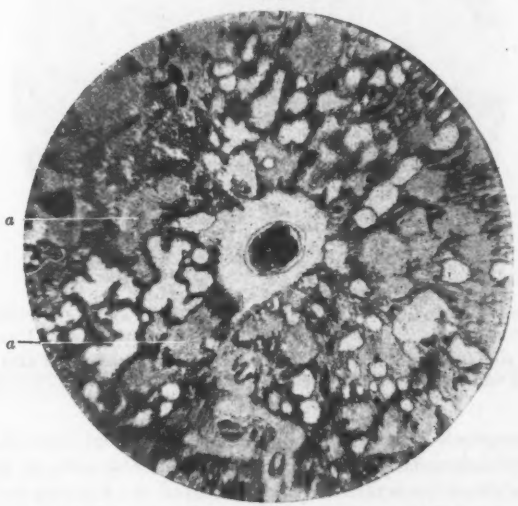
such animals numerous necrotic pseudotubercles were found in the lungs, liver, kidneys, heart muscle, and on the surface of the

FIG. 1.



This shows the twisted branching threads when stained from a culture of actinomyces asteroides by Gram's method.

FIG. 2.



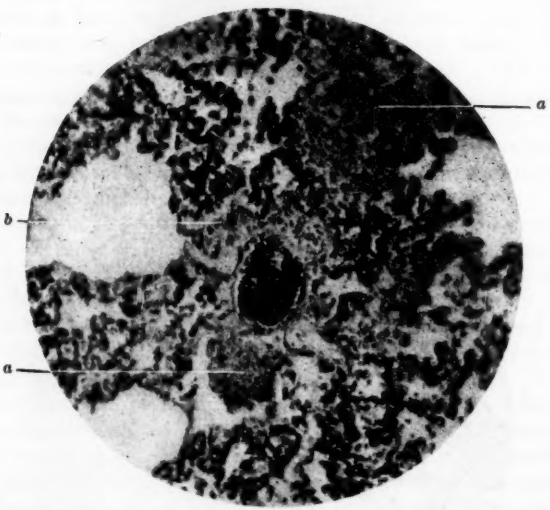
This is a picture of the lung of an injected guinea-pig when seen under the low power. In the centre is an artery, and below is a bronchus and several bloodvessels. The dark areas throughout the section are the pseudotubercles produced by the injection of the organism into the pleural cavity, the figure showing a necrotic nodule to the left of the artery, and another to the left of the bronchus (see "*a*").

various serous membranes. MacCallum did not find the typical production of lymphoid and epithelioid cells which precede necrosis

of the true tubercle, due to B. tuberculosis, but he found that the connective-tissue cells proliferate later and form a capsule of granulation tissue, which often contained giant cells. Our own experimental lesions often showed a similar proliferation of connective-tissue cells, in which small lymphocytes were often present. The photomicrographs show the various proliferating cells and the necrotic pseudotubercles in the lungs and heart.

Actinomyces asteroides thus produces a primary exudation of leukocytes, and, of course, organisms from the capillaries. In rabbits and guinea-pigs this is followed by necrosis and encapsulation of the injured tissue by a proliferation of the fixed tissue cells.

FIG. 3.



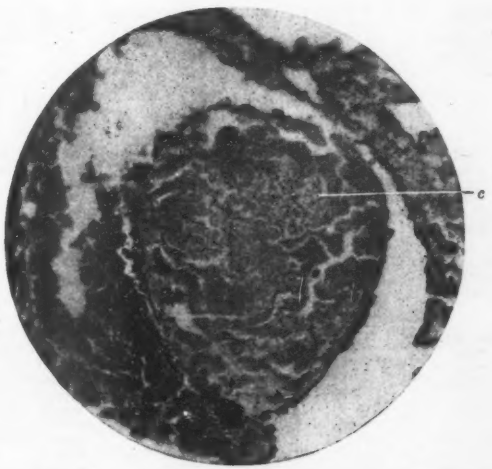
This shows several tubercles at *a*, and *b* indicates the proliferation of the fixed tissue cells around a vein in the centre of the picture. This is the final reaction to the organism.

Actinomyces Vesicæ. Through the kindness of Prof. Hugh H. Young, of Johns Hopkins University, I am also able to report an organism which he isolated by aspiration of the bladder in the case of a man, aged sixty years, at the Johns Hopkins Hospital.

The patient was suffering from chronic nephritis and uræmia, with retention of urine. About 1500 c.c. of urine were aspirated from the bladder, and much pus was found in this fluid. In addition a bacillus which could not be identified as any pathogenic organism was isolated, and an organism with long threads and true dichotomous branching was isolated in pure culture. This organ-

ism was called actinomyces vesicæ, and, as its cultural characteristics are completely described in the accompanying table, these will not be repeated at this time. Its main characteristic is the brilliant orange color that it produces in cultures, but it can be distinguished from the actinomyces asteroides by the fact that it liquefies gelatin, casein, and blood serum. It did not prove pathogenic when injected into guinea-pigs, either subcutaneously or in the pleural cavity, and it cannot be claimed that it caused the cystitis noted above. It is probable that it did, however, since a saprophytic bacillus was the only other organism found in the purulent urine, and it is embraced in this study with the expectation that it may be noted in other pathogenic processes.

FIG. 4.



This figure shows a section made through a papillary muscle of the left ventricle. The red blood corpuscles can be seen free in the cavity and surrounding the muscle, and the central portion of the papillary muscle contains a necrotic pseudotubercle produced by injection. The normal muscular structure and the necrosis and fragmentation of the pseudotubercle can be well made out.

CLASSIFICATION OF THE VARIOUS SPECIES OF ACTINOMYCETES. On reviewing the literature concerning the various species of pathogenic actinomycetes it became apparent that several of the species described by different authors could be grouped as one species on account of their similarity. This classification has already been made by Silberschmidt, but the accompanying table includes species not described by him, as well as the pathological changes in men and animals. A few of the organisms have not been described completely enough for classification, but those which have been thoroughly described can be grouped as seven distinct species.

Name of organism and observers.	Morphology.	Motile.	Spores.	Gram's stain.	Metachromatic bodies.	Appearance on agar.	Appearance on blood serum.	Appearance on potato.	Gelatin plate.	Growth in bouillon.
Actinomyces bovis. Bollinger, Israel, Boström, and others.	Ray fungus consisting of a radiating mass of mycelium containing many spores in centre, showing evidence of true branching forms; at the periphery the threads terminate in clubbed ends.	0	+	+	0	Small opaque colonies which later show a white downy appearance, which coalesce into an adherent, wrinkled, lichen-like membrane.	Same as agar; the blood serum liquefied.	Same as agar; the growth is slower and is of a yellowish color with a white shaggy deposit.	Arborescent colonies which slowly liquefy gelatin.	Opaque globules like grape seeds which coalesce into a loose flaky sediment; no surface membrane forms.
Actinomyces asteroides. Eppinger, McCallum, Sabrezes et Rivière(?), Aoyama, Stokes, Berestneff.	Mycelium with branching threads ending in spores of an elongated appearance, and also showing clubbed ends.	0	+ Staining by the Ziehl-Gabbett spore stain.	+	+ Neisser's stain.	Small shaggy colonies which coalesce into a thick adherent membrane with elevations and depressions and of an orange color.	Same as agar; serum not liquefied.	A profuse white or yellow growth with a fine white feathery growth from upper surface.	Small, radiating colonies near surface with depressed centre and shaggy margins.	Beginning as minute, white shaggy colonies like puff balls, they form a dense elevated and depressed yellow surface membrane on surface.
Actinomyces Israelli. Wolf and Israel, Norris and Larkin, Levy, Aschoff.	Short branching mycelium, with bulbous or clubb'd ends and coccus-like spores.	0	?	+	+	White pinhead sized colonies of a conical shape, not often coalescing.	Scanty white growth; very adherent.	Not observed.	Pinhead, later spreading colonies of whitish opaque colors.	Small discoid fluffy granules, often adherent to sides of tube.
Actinomyces Nocardi (du Farcin du Bœuf). Nocard.	Long thin hyphæ twisted in masses, showing many branching forms like cabbage sprouts or burs.	0	+ Resist ordinary stains	0	Not mentioned.	Small, white irregularly round, opaque colonies which form an adherent, thick, wrinkled membrane-like lichen.	Same as agar, but moister in appearance.	Grows rapidly as small, scaly plaques, which form a projecting dry pale yellow growth.	Not observed.	Irregular white masses which fall to bottom of tubes, but a gray lenticular membrane forms on the surface; no change of neutral or alkaline sugar bouillon.
Actinomyces Maduræ. Vincent.	Many twisted filaments showing true branching forms, and staining irregularly. The mycelium shows a ray-like growth at the periphery, but no true club forms; some of the hyphæ show nodular enlargement along their course.	0	+	+	+	Small, projecting, round whitish-yellow colonies, which slowly take on a rose color; they show an umbilication in the centre and become confluent and adherent to the medium.	Do not develop on blood serum.	On the fifth day at 37° C. numerous small white colonies appear with a mammillated aspect; the growth remains white.	Small colonies with a filamentous periphery; no liquefication of medium.	Small, floating, independent zoogleal, white balls, which slowly sink to bottom of tube.
Actinomyces capræ. Silberschmidt	Twisted branching filaments which break off at the end into forms resembling bacilli or cocci; a few of the shorter forms show clubbed ends.	0	+	+	Stains irregularly.	In two or three days dry, verrucose, shrivelled, brownish-white colonies appear which form an adherent, brown, irreg'lar membrane in from eight to fifteen days.	Colonies in four to eight days which form a dry brown coat.	Round, dry, crater-like colonies which later form a pinkish brown coat on the surface.	White colonies with a dense brown centre, and a clear periphery showing many projecting filaments.	Colonies develop on surface as concave, fine, dry, pale disks which later form a surface membrane; fluid clear, but a deposit forms in the bottom of tube.
Actinomyces vesicæ. Young.	Mycelium twisted, showing irregularity in size and staining; a few ovoid gonidia growth from side of hyphæ which show true branching forms.	0	0	+	0	Brilliant orange-colored groups like seed often piled on one another, resembling a cone; very adherent to agar.	Same as agar; serum slowly liquefied.	Brilliant orange-colored adherent growth.	In three days many round orange colonies with finely granular centre and many projecting threads under low power.	Large, pale-yellow balls with orange centre and fine fuzz on surface.

Fermentation tube; glucose.	Liquefaction, gelatin, casein, serum.	Gelatin stab.	Nitrate reduced.	Indol production.	H_2S.	Litmus milk reaction.	Chromogenesis.	Pathogenesis.
No fermentation of glucose; aërobic.	Liquefies serum, casein, and gelatin.	Arborescent growth which liquefies gelatin.	Positive marked reaction.	Well-marked reaction after standing for 24 hours.	+	Dirty yellow membrane on the surface; reaction alkaline.	Slight yellow color.	Pathogenic for bovines and human beings; producing a subacute, diffuse, purulent inflammation, with the formation of granulation tissue
No ferment. or growth in closed branch; thick typical yellow-white, elevated and depressed membrane on surface of open branch; aërobic.	0	No liquefaction; growth arborescent.	Very slight reaction.	Very slight reaction: Sabrezes et Riviere. 0	+ Sabrezes et Riviere 0	Thick yellow elevated and depressed membrane on surface; reaction alkaline.	Orange yellow color; Sabrezes et Riviere light yellow to chocolate brown.	Subcutaneous injections produce purulent abscesses, and injections into circulation or serous cavities produce necrotic nodules in the various viscera of rabbits and guinea-pigs; the organism produces purulent inflammation in human beings. Sabrezes et Riviere 0.
No ferment, growth in both arms; facultative anaërobic; grows only at 37° C.	Casein not liquefied.	No growth at 20° C.	0	No growth in Dunham's solution.	.....	Acidulated and coagulated.	0	Intraperitoneal injections produced necrotic nodules in the peritoneal cavity and viscera containing the actinomyces; often these nodules contained purulent centres surrounded by a zone of granulation tissue. Same as A. bovis for human beings.
No fermentation, and only grows in the open branch; anaërobic.	0	No liquefaction.	Not observed.	Not observed.	0	No coagulation or acidulation; remains neutral.	0	In bovines the organism produces purulent inflammat'n of lymphatic glands; intravenous or intraperitoneal injection into guinea-pigs causes the formation in viscera and peritoneal cavity of many small nodules which contain pus and the organisms; subcutaneous injection produces pus formation
No fermentation growth in open branch; aërobic; no growth in a vacuum; CO_2 or H.	Gelatin and blood serum negative; casein dissolved	Abundant white growth along track of needle; no liquefaction.	Not observed.	Not observed.	Not observed.	Coagulated and later the casein is dissolved	Light yellow to red on agar.	Not pathogenic for laboratory animals; in human beings the organism produces a pseudotubercle of the extremities consisting of a central zone of mycelium infiltrated by polymorphonuclear leukocytes surrounded by a second zone of regenerating tissue containing fibroblasts, newly formed capillaries, and masses of red blood-corpuscles.
No fermentation.	Gelatin, blood serum, and casein not liquefied.	Not described.	Not observed.	Not observed.	Not observed.	Not coagulated; rose colored membrane on surface.	Varies from white to rose color and brown.	Subcutaneous injections caused purulent abscess in guinea-pigs and rabbits, and intravenous injections produced generalized tubercles which contained giant cells and underwent caseation. Isolated from the lung of a goat containing many pseudotubercles.
No gas formation, aërobic and facultative anaërobic.	Liquefies gelatin, casein, and blood serum.	Fine light orange line.	Marked reaction.	0	0	Reaction acid.	+ Bright orange color.	Guinea-pigs injected subcutaneously and into pleural cavity were observed for one month and then killed; no lesions were found.

Actinomyces bovis can be distinguished from four of the other species by its failure to infect small laboratory animals, and from actinomyces Maduræ by the failure of the latter to liquefy blood serum or gelatin. The anaërobic species, actinomyces Israeli, can be distinguished from all other species by its preference for an anaërobic medium, and especially from actinomyces bovis by its production of necrotic pseudotubercles in guinea-pigs and rabbits. Actinomyces asteroides can be easily separated from actinomyces bovis by the failure of the former to liquefy blood serum and gelatin, by its bright golden-yellow appearance, and by the production of pseudotubercles in laboratory animals. It also differs from actinomyces Nocardi in its yellow color, and in producing an alkaline reaction in milk, while the latter remains neutral and white. Actinomyces Maduræ differs from actinomyces capræ by the former's failure to infect small laboratory animals, by the rose color of the former, and the brown color of old cultures of the latter, and by the liquefaction of casein by actinomyces Maduræ. Practically all of the species described (see table) can be placed in these seven groups.

Chemical Products of Actinomyces Asteroides. MacCallum attempted to produce a soluble toxin from cultures in bouillon about three weeks old. These were filtered through a Pasteur filter, and the filtrate, in doses of from 6 to 10 c.c., was injected into rabbits without any ill effects. The writer grew this organism for one month in neutral bouillon and then filtered it through the Pasteur filter, and preserved this fluid by 0.5 per cent. carbolic acid.

Two guinea-pigs, weighing about 300 grams, were injected with 0.5 and 0.1 c.c. of the fluid, and they died in ten days. The lungs were congested, and microscopic examination showed intense congestion of the lungs, liver, and kidneys. Two more guinea-pigs were injected with 0.1 c.c., and one died in twenty-four hours. The seat of injection, the liver, and the lungs were all congested. The other pig remained well.

These experiments indicate that the organism forms a soluble poison for guinea-pigs.

Conclusions. The various forms of pathogenic actinomycetes can be classified at present as seven species, which produce suppuration or necrotic pseudotubercles in man and various animals.

The generic name for this group should be actinomyces, since the other names have been previously used for other organisms.

Cases resembling tuberculosis but failing to show tubercle bacilli should be carefully examined for the presence of actinomyces.

In concluding, I desire to thank Mr. John Johns and Dr. John S. Fulton for the photomicrographs, and Dr. Caleb Rohrer for assistance in the pathological study.

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ASSOCIATED MOVEMENTS OF THE HEAD AND EYES IN INFANTS.[1]

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AND

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THE various forms of movements of the head and eyes in infants —the so-called rotary and nodding spasms of the head and vertical, horizontal, and rotary nystagmus—are observed quite commonly. The obscurity of their origin makes them especially interesting. For this reason Dr. Posey and I have decided to present these three cases, which happen to be attending our services in the Howard Hospital at the present time.

CASE I.—Carl C., aged three years, first came to the children's clinic in the Howard Hospital on October 13, 1903. The history recorded at that time was as follows: His birth was normal, and his first dentition complete. His parents are living and well, save that his mother is thought to be nervous. He has no brothers nor sisters, and his mother has had no miscarriages. His previous health has been excellent. He has had none of the infectious diseases of

[1] Read before the Philadelphia Pediatric Society, April 12, 1904.

childhood, and has never had any convulsions. For some time he has complained of abdominal pain. For many months he has lived chiefly on two cups of weak tea with each meal, milk, bread, and butter. He never eats meat. He eats freely of ice cream, but of other sweets rarely.

The condition which brought him to the dispensary was a cough of two days' standing which was accompanied by fever at night. The cough had a tendency to be paroxysmal, and the paroxysms were sometimes severe; it was tight, and there was no expectoration. He had some epigastric pain, and his bowels had been loose for several days. He had several stools each day, which were yellowish and watery, but contained neither blood nor mucus.

The physical examination showed a well-nourished child. His tongue was heavily coated, and its papillæ red and prominent. His frontal and parietal eminences were prominent; there was moderate thickening of the epiphyses at the wrists and ankles. There was some costochondral thickening and some retraction of the base of the chest, more marked on the right side; there was moderate dorsolumbar lordosis and decided outward bowing of the tibiæ. His abdomen was prominent; its walls flaccid, and there was marked separation of the bellies of the recti. His spleen was not palpable, but his liver was felt a finger's breadth above the transverse umbilical line, about three inches to the right of the umbilicus. There were a few scattered moist rales over each lung. He had a fairly loud, low-pitched, blowing systolic murmur, best heard in the aortic area and transmitted especially well to the top of the sternum and into the subclavians, less well into the carotids. A murmur of similar character was heard over the body of the heart, at the apex, in the axillary region, at the angle of the scapula, and in the interscapular space. At the apex the murmur was the same in character as that heard at the base, but in this area it seemed to occur later in systole; the second sound was heard distinctly over the upper chest.

On November 15th he had a mild follicular tonsillitis. On March 10, 1904, he was brought to Dr. Posey's clinic in the Howard Hospital on account of movements of the head and eyes and reduction in vision. These manifestations were first noted early in December. They had increased persistently up to this date. The head movements were lateral and not constant, the head apparently being drawn to the right and the chin slightly elevated, as if by action of the left sternocleidomastoid muscle. The eye movements were also from side to side and constant, the excursions being fairly extensive.

He was unable to recognize objects at a distance of four or five feet, but when brought within this range they could be defined. Any attempt at fixation caused a decided increase in the excursions of both the head and eye movements, especially the latter. Covering the eyes produced a temporary cessation of the movements of

the head, and they ceased during sleep. There was some restriction to the movements to the right in both eyes.

An examination of the eye-ground by Dr. Posey showed some engorgement of the veins, but no other abnormality. The only other nervous phenomenon noted was a slight uncertainty in his gait, and a mild ataxia, which had never been sufficiently marked to attract the father's attention. His reflexes were normal.

Further questioning showed that in December he had had a slight discharge from one ear, which cleared up quickly. About the same time he developed a cough, which has persisted. He has occasional severe paroxysms, which the father says sound like whooping-cough. Usually it is loose, but without expectoration. He vomits during or immediately after almost every meal. He does not seem to be nauseated, and frequently eats immediately after vomiting without being sickened. He never vomits at other hours of the day. His bowels continue loose—four or five stools each day—which are watery and yellowish in color. He voids urine frequently and in large quantity. Two examinations of the urine showed nothing abnormal, except a lowered specific gravity —1014 and 1012. Dr. F. R. Packard kindly examined the ears, throat, and nose, and reported nothing abnormal.

Case II.—R. E., aged seven months, came to the Howard Hospital Dispensary on March 24, 1904. His birth was normal; his parents, three brothers, and one sister are living and well. One brother died aged two years of "baby consumption." He has had no convulsions, no manifestations of syphilis, and no previous illness. He has been fed exclusively on the breast about every third hour.

He was brought to the dispensary on account of a coryza of one week's duration; the discharge was free, and consisted of thin mucus without blood. His respirations were snoring in character —a condition which had existed since birth. There were no evidences of sore throat, but he had a cough in the beginning of the attack which was croupy in character. He has had no gastro-intestinal symptoms.

The mother first noticed shaking movements of his head and eyes between the third and fourth months, and for some time he has had profuse head sweating. He is thought to have gained steadily in weight. He has always been a mouth-breather, and constantly chokes while nursing, as if there was some obstruction to nasal breathing. He seemed quite bright, and had no fever.

The physical examination showed a fairly well-nourished infant. There was no evidence of nasal membrane. His uvula was swollen and red. The fauces and tonsils were red, but without exudate. His tongue was moderately coated. His head was narrow in the bitemporal diameter, and the posterior fontanelle was still open. The coronal, sagittal, and lambdoidal sutures were wide open, and there was marked craniotabes along the borders of the squamo-

parietal and mastoparietal sutures, especially evident on the right side. He had a bald spot over the occiput. His neck was short, and the sternum elevated. His clavicles were on a direct plain with the body, and probably elevated slightly at the sternoclavicular junctions. His chest was markedly violin-shaped, his costochondral junctions were much enlarged, suggesting on palpation a backward dislocation of the cartilages. The portion of the chest wall between the costochondral junctions was pushed forward. The epiphyses were thickened at the wrist and knees, and there was slight dorsolumbar kyphosis. His abdomen was prominent, the bellies of the recti muscles were separated, and there was some pouting of the umbilicus. He had a frequently recurring spasm of the muscles of the back of the neck, with retraction of the head. Similar muscle spasms were not noted in other groups. His inguinal, axillary, epitrochlear, suboccipital, postcervical, and a few of his deep cervical glands were enlarged. He had marked lateral and tilting to-and-fro movements of the head, the head rotating to both sides as if by alternate contractions of the sternocleidomastoid muscles.

Dr. Posey's report upon the eye condition showed "lateral nystagmic movements with very short excursion and of similar extent in each eye. There were no apparent ocular palsies. On near fixation the movements were much increased, and this was associated with increased movements of the head. The examination of the eye-ground showed nothing abnormal."

On April 8th it was noted that the infant had emaciated decidedly, although his general condition seemed better; his head and eye movements were less.

Case III.—Lilian B., colored, aged eleven months, applied for treatment at the Howard Hospital Children's Dispensary on August 13, 1902. Her birth was normal.

Family History. Both parents are living and well, but a paternal aunt and uncle died of phthisis. The child had had no previous disease, but had always been "poorly." She had been breast-fed for the first four weeks of life, since which time she had been fed on cows' milk, bread, crackers, cakes, candy, ice-cream, chocolate, and potatoes. She was brought to the dispensary for a cough, which she had had for three or four months. She was sometimes feverish, and had occasional night-sweats. Her cough was most severe at night. Her bowels moved six or seven times a day, the stools being yellowish in color, very loose, malodorous, and containing curds, but no mucus.

Physical Examination. The child was emaciated. The anterior fontanelle was very large, the sutures open, and the posterior fontanelle still open. The chest was markedly violin-shaped, and there was beading of the ribs. There was some epiphyseal thickening, the abdomen was very prominent, the umbilicus pouted, and there was separation of the bellies of the recti muscles. The

heart's action was regular and rapid, and the sounds clear. The breathing was labored, and the respiratory movements were increased in frequency. There were no areas of dulness. There was a wheezing sound on inspiration. The chest was full of sibilant and sonorous rales, by which the respiratory murmur was masked. There were no areas of bronchial breathing. The spleen was palpable just below the costal margin, and the liver one-half inch below. The cervical, anterior and posterior, the axillary and inguinal glands were moderately enlarged. The body temperature was normal.

The child made three return visits from this time up to the middle of October, 1902, and then disappeared until February 24, 1903. She was brought back on account of the return of the cough of the previous winter. She had recently had an otitis media on the left side. At the time she returned she was having a great deal of nasal discharge. Her appetite was poor, her cough loose, and attended by considerable expectoration. She slept well, but sweated a great deal about the head at night. It was noted at this time that she had a marked lateral nystagmus, which was said to have existed since the third month. It was much more marked in the right eye, and was at first thought to have been unilateral. There was no history of head movements at any time, nor of muscular twitchings in any other part of the body. At the age of sixteen months she had only her upper and lower middle incisor teeth. The anterior fontanelle was as large as a dollar, and the sutures were separated some distance from the fontanelle. There was marked bowing of the bones of the forearm, eversion of the legs, without much bowing of the bones, except a slight anterior bowing of the tibiæ. The spleen was palpable a finger's breadth below the costal margin. The child was very weak, and required considerable assistance in order to maintain an erect posture. There were a few rales over the chest. The physical examination otherwise showed no changes.

Following this the child was absent from the dispensary for about eight months, when she returned with an aphthous stomatitis. Five months later she returned suffering from prolapse of the rectum. She was having three or four stools daily, accompanied by straining. They contained mucus, and there had been a slight amount of blood in some stools. This developed sometime after the prolapse of the rectum. Prior to this time the bowels had been normal. The abdomen was very much distended. There was no vomiting. The spleen was not palpable, the liver was two inches below the costal margin. There was no evidence of prolapse of the rectum found on examination.

The child returned twice following this, the last time on March 30th, on which occasion it was announced that there was no longer any prolapse of the bowel. A careful physical examination showed nothing to account for the prolapse. She had never vomited. She had no abdominal signs of any significance.

She is twenty-six months old at the present date. Her eye and stomach teeth are just erupting. All of her teeth are in poor condition and immaturely developed. One lower incisor has been lost by being caught in the thread of her skirt, indicating that the attachment of the teeth is insecure. The examination of the eye condition by Dr. Posey shows that when at rest the nystagmus is limited to the right eye; the movements are lateral, and the excursions very short. On fixation, or when the eyes are removed from the primary positions, slight nystagmic movements appear in the left eye also. There does not seem to be any limitation in the movements of the eyeball in any direction. Once or twice during examination, when the attention was suddenly attracted, there was a marked vertical vibrating spasm of the upper lids. Excitement increased the nystagmic movements, but the movements were not increased when the head was held fixed.

The question of the *etiology* of these phenomena remains unsettled. Numerous theories have been advanced, and the more recent writers have been in some accord in relation to this point. That the condition is dependent upon some functional disturbance of that part of the nervous system controlling the movements of the head and eyes is generally conceded. While it is not our purpose to treat this subject exhaustively it may be well to briefly review some of the more important theories that have been suggested.

Predisposing Causes. Age is an essential predisposing factor, the vast majority of cases occurring between the ages of two and twelve months, although Gee has reported a case occurring as early as the sixth week, and Henoch one as late as the third year. The cases are pretty evenly divided among the sexes with a slight majority in favor of females.

Heredity is supposed to play some part, in that a number of cases have occurred in families of bad nervous history, including epilepsy.

Rickets is probably the most common predisposing factor. In his early series of cases Hadden found this condition present in but two of eleven. On the basis of this finding he attached but little importance to it. In his second series of nine cases he found it present seven times, after which he modified his views decidedly. Other authorities differ as to its etiological relationship, the majority considering it an extremely common factor. The remarkable frequency of rickets, especially of its milder forms, would lead us to believe that its association has probably been closer than statistics would indicate. We are of the opinion that the milder manifestations of rickets, the head sweating, delayed dentition, and moderate beading of the ribs, but more especially the muscle and nervous phenomena, are of very frequent occurrence, and that, because we are prone to depend upon the skeletal deformities for our diagnosis, the manifestations in the nervous system—irritability, night terrors, etc.—and the muscle phenomena—pot-belly, gastric and intestinal

distention, constipation, etc.—are apt to pass unrecognized. In the dozen or more cases seen by one of us rickets of some degree was manifest in each.

Exciting Causes. Dentition was thought by Henoch to be the most common, because the conditions occurred during the period of first dentition, and because in some of his cases its beginning was coincident with the eruption of some of the first set of teeth. Most authorities admit that it may act as a contributing cause, but that it does not occupy the important position attributed to it by Henoch is manifest from the fact that many recorded cases have occurred at an age which would eliminate the teeth as a disturbing element.

Gastrointestinal irritation has preceded its occurrence in many cases, and it is generally conceded to be an important factor. It may act either reflexly or through the medium of toxic products absorbed from the intestinal tract.

Traumatism was recorded in a number of Hadden's cases, and in those of Peterson and Hirsch. Peterson thinks it probable that concussion is the determining factor in most cases—"a concussion setting up in the centres of the spinal accessory, and at times in those of the oculomotor nerves, an arrhythmic discharge."

Our knowledge of the pathology of these movements, for obvious reasons, is mainly speculative. Hughlings Jackson considered the condition a variety of "spinal system chorea, a symptomatic condition akin to canine chorea," while Gunn believed it was in some way associated with epilepsy, basing his view upon the quite common occurrence of temporary loss of consciousness in these cases, and the presence of epilepsy and other nervous conditions in the families in which they occur. Henoch previously suggested the same view, and Hadden, whose cases were the basis of Gunn's suggestions, gave this opinion some consideration.

Henoch, in describing his cases, suggested that the concomitant existence of these head-and-eye movements "seem to indicate that the root nuclei of the spinal accessory and of the upper spinal nerves supplying the affected muscles of the throat and neck stand in a very close relation to those of the ocular nerves (occulo-motorius)," a relationship which has since been definitely determined. Hadden believed that "the seizures pointed to instability of motor centres above the nuclei in the spinal cord and fourth ventricle, therefore attributing the disorder to a functional or other disturbance of the cerebral cortex. The child has acquired certain voluntary or purposive movements of the head and eyeballs, but these have not as yet become thoroughly organized and fixed in the psychomotor areas of the brain, hence a dissolution takes place because of the inability of the strained cortical centres to stand the work to which they have been too early subjected." This opinion, quoted by Mills, is one which he believes "throws the best light on an obscure subject."

Aldrich, in his very able discussion of this condition, voices the same view as to the nature of the condition. As we have stated, while we are by no means certain that the nature of these conditions is definitely determined, we incline to accept Hadden's explanation.

These three cases differ to some extent in the character of the head and eye movements. In Case III. the head movements are lacking entirely, the nystagmus is mainly in the right eye, and, according to the mother's statements, has existed since the third month. A point of special interest in this case is the occurrence of the vertical movements of the upper eyelid on an attempt at sudden fixation, a feature which has been noted but once before.

In Case II. the movements began at a very early period—between the third and fourth months—and involved both the head and eyes. They were equal on both sides. There was present in this case an intermittent spasmodic contraction of the muscles of the back of the neck.

In Case I. the movements began at an unusually late period—after the time that such movements have ordinarily disappeared. The head movements in this case are caused mainly by spasmodic contraction of the left sternocleidomastoid muscle, and the eye movements are the same on the two sides. In addition, there is some evident defect of vision and a slight ataxia, a somewhat similar condition having been noted in one of Hadden's cases. This is the only case in which it was possible for us to demonstrate any limitation in the excursions of the extraocular muscles.

Strabismus was not noted in any of the cases. There have been no antecedent nervous conditions from which the head and eye movements might have resulted, and none of them have had any of the acute diseases of childhood except Case I. The pupils were of normal size and reacted normally in all three cases, nor were there any changes in the fundi other than the dilatation of the retinal veins noted in Case I. The eyes in all three cases were moderately hypermetropic.

While the head-and-eye movements are manifested in a somewhat different way in each of these cases, and while we have been unable to elicit a history of head movements in one of them, we are, nevertheless, of the opinion that they are all dependent upon some form of irritation of the cortical areas.

The extreme rachitic manifestations present in all the cases marks this condition as the underlying or predisposing factor. The exciting cause in Cases II. and III. are difficult to determine. They both developed before the age of dentition, there is no history of injury, and they did not suffer from acute diseases which might have acted reflexly or by the development of some toxic irritant, or by suddenly producing increased instability of the motor centres, from the resulting exhaustion. The early age at which they became

manifest and the striking rachitic condition which was present lead us to believe that the toxic products resulting from the disturbed metabolism due to the rickets were the irritating factors in these cases. In Case I., however, the conditions are different. The rachitic manifestations in the child were much later, but very marked, quite sufficient to interfere with the nutrition of the nervous system.

The movements began in this case about two weeks after an attack of bronchitis, which was associated with diarrhœa, the latter condition persisting up to the present time. Furthermore, this child has been partaking most intemperately of tea for many months, regularly drinking two cups with each meal. The bronchitis, diarrhœa, and tea drinking, therefore, acting in a markedly rachitic child, we consider quite sufficient to have produced the phenomena noted.

A point of interest in these cases is the relationship which exists between the movements of the eyes and head. In an article which was read by one of us before the fifty-third annual meeting of the American Medical Association, entitled "Associated Movements of the Head and Eyes," the close association which exists physiologically between the movements of the head and eyes was dwelt upon, and it was shown how the head by its movements augments the range of the field of vision and supplements the action of the extraocular muscles in the delicate task of maintaining proper visual axes. Attention was also called to the fact that in order that the head may properly perform this twofold task it is provided with numerous and intricately acting muscles, and it is only when one considers that there is scarcely a position assumed by either the eyes or head in which the action of both parts does not enter that one realizes how intimate the relationship between the extraocular and cervical muscles is.

To facilitate the study, all associated movements which exist between the head and the eyes were divided into four groups. The first group referred to movements which are physiologic and will require no further mention here. The second group included abnormal simultaneous but independent movements, such as occur, for example, in disseminated sclerosis, where the movements which are abnormal and often simultaneous and have the same pathogenic origin are not related in the sense of being dependent upon one another. The third group dealt with compensatory movements. To this class were relegated cases which assumed a vicarious position of the head to compensate for some imperfect action of one or more of the extraocular muscles, such, for example, as occur after paralysis of one or more eye muscles. The fourth group referred to related but not compensatory movements, and included movements of the head and eyes which are abnormal and bear a distinct relationship to one another without being dependent upon

one another. Cases of head-nodding in children, such as have been presented to the Society to-night, were included under this latter group, although it was realized that there are a number of reasons why they should have been placed under the third group and the movements of the head considered to be secondary to those of the eyes. Thus, it is a well-established clinical fact that movements of the head, apparently similar to those observed in this class of cases, may originate in children whose eyes oscillate as a consequence of lowered vision, occasioned by a disease of the eyes, and it has been noted not infrequently that nystagmic adult patients hold their heads in a peculiar position while fixing for both distant and near objects, and often succeed in steadying the oscillation of the eyeballs in this manner. It has been remarked, too, in cases of the affection under discussion, by both Raudnitz and Caillé, that if the eyes are bandaged the motion of the head ceases. Raudnitz noted also, in common with other observers, that the head movements were much influenced by the deviation of the visual axes, that they ceased when the eyes were deviated in certain directions, and started up again as soon as they were rotated from this position. This writer thought that the disease was particularly apt to arise in the dark winter months and to affect those confined in darkened rooms, believing that the head-jerking was secondary to the nystagmus, the latter being occasioned by strain upon the eyes consequent upon the infant's constant attempt to look toward the windows. Notwithstanding these observations and the well-established fact of the possibility of movements of the head being inaugurated by those of the eyes, it is probable that such is not the case in head-jerking, the movements occurring in association by reason of a common cause affecting the centres controlling each simultaneously, but without being dependent upon one another.

While in most instances the data which have been gathered regarding the time of the occurrence of the nystagmus and of the head-jerking are obtained by questioning the parents, and are, therefore, not entirely reliable, still there is evidence to show that the nystagmus does not always precede the head-nodding, that the head-nodding may even be observed some weeks or months before the jerking in the eye muscles manifests itself, and that, finally, head-jerking may occur without the occurrence of nystagmus during the entire course of the disease.

Moreover, in order that the movements of the head should compensate and neutralize those of the eyes, they should be directly opposite to one another; such a condition, however, has been found in but one case, the motion of the head being either in the same direction as those of the eyes, or, what is more usual, without any connection with them whatsoever. Again, the movements of the eyeballs are usually twice as rapid as those of the head and have their own rhythm.

It has been suggested that the presence of a strabismus in some of these cases would indicate that the nystagmus, under such conditions, at least, was the primary factor, but while the strabismus may indicate a palsy of one of the eye muscles nystagmus does not follow palsy of the eye muscles under other conditions.

A STUDY OF A CASE OF SPLENOMYELOGENOUS LEUKÆMIA.

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(From the medical service of Dr. Wainwright.)

The subject of this study was previously under the care of Dr. J. Emmet O'Brien, of Scranton, and Dr. Thompson, of Carbondale, to both of whom we are indebted for notes of his former history.

The patient stated that about six years before admission to the hospital he had a severe attack of abdominal pain, with vomiting and diarrhœa. He said that this illness was similar to his subsequent ones. He was given arsenic at the time, and made a good recovery, and was apparently in good health until late in the year 1902, except for a time in 1901, when he was bothered by a pain in the splenic area.

About October, 1902, he began to suffer again with "bloating" and with alternate constipation and diarrhœa. Dr. O'Brien first saw him on December 11, 1902. He found the spleen much enlarged. A record of the blood count was not kept, but it is known that the leukocytes were much increased in number, and smears showed the picture of a leukæmia of the splenomyelogenous type. Fowler's solution in increasing doses was prescribed. On January 3d the patient returned much improved, and the splenic tumor was not palpable. On January 28th the spleen could again be felt, and the leukocytes were still numerous. His general condition, however, seemed to be improved. He was last seen by Dr. O'Brien on March 24, 1903.

From March, 1902, until his admission to the hospital he was seen a few times by Dr. Thompson, who was called chiefly for gastrointestinal trouble. One of these attacks yielded to small doses of calomel daily. At another time he was again given arsenic, with benefit.

On the whole, during this period his condition was fairly good, He seems to have been troubled only by the attacks of diarrhœa, and he kept very steadily at his active duties as inside foreman of a coal mine until March 31, 1904.

The patient was admitted to the Moses Taylor Hospital on April 14, 1904.

Family History. Father died of miners' asthma[1] at the age of sixty-six years. Mother well at sixty-eight. Grandparents died of old age. Has one sister, aged forty-six years, and one brother, aged forty years. Both have always been well. One brother died of violence at the age of twenty-six years. He has been married twenty-one years. Wife is well. He has seven living children, all of whom are well. Three other children died in infancy of convulsions, diphtheria, and enteritis, respectively.

Personal History. He is forty-one years old. Was born in Wales. Came to this country when two years old. At ten he started to work in a coal breaker. At eleven he began to work inside the mines as a driver boy. He was for many years a miner, and for the last fifteen years has been inside foreman. He has worked continuously inside the mines for thirty years.

He has used alcohol and tobacco only in moderation, and denies venereal infection. There is no history of malaria.

Present Illness. In addition to the notes above he stated that while he did not give up work until two weeks before admission he had been gradually growing weaker for the past seven months, His only complaints have been a feeling of tightness in the epigastrium, "swelling of the stomach, which made him short of breath," and frequent attacks of vomiting and diarrhœa. About a week ago he began to have severe occipital and frontal headaches. For four months his feet have been slightly swollen, and for several months he has had a dry cough.

Physical Examination. An emaciated man of small stature, looking ten to fifteen years older than his correct age. There is a marked general pallor of the skin and mucous membranes, with a slight yellow-lemon hue. There are no hemorrhagic areas visible. The throat looks normal except the tonsils, which are a little reddened and swollen. There is no stomatitis. The muscles are small and flabby, and there is very little adipose tissue. Pulse, 100; temperature, 99°; respirations, 24.

Thorax. This is rounded and thickened anteroposteriorly. Its lower portion is bulged forward, forming a well-marked Harrison's groove on both sides. Lungs normal. The heart is either enlarged or displaced upward. The dulness from the upper border extends to the second interspace; the right border to the right edge of the sternum. The apex beat is felt in the fourth space one inch to the left of the midclavicular line. The first sound at the apex is weak; the second aortic is slightly exaggerated.

[1] This is a term which is very loosely used in the coal regions and covers almost anything in the way of chronic bronchitis, emphysema, myocarditis, chronic nephritis, phthisis, or even the general failure of old age.

The arteries are prominent and tortuous and markedly thickened. The pulse is full and firm. Tension is not raised (132 mm. in radial by Riva-Rocci).

Abdomen. The left costal margin is bulged forward more than the right, and there is a visible tumor in the left hypochondrium. On palpation this tumor is evidently the spleen. The spleen is stony, hard, and smooth; the edges are sharp and well defined, but no notches can be felt. At this time the mass is not painful or tender. The upper border of splenic dulness is at the sixth space in the anterior axillary line. The right edge is felt one inch from the median line, and the lower margin is on a level with the antero-superior spines. The liver is also considerably enlarged. The dulness of the upper border begins at the fourth rib in the mid-axillary line. The lower border can be felt about one inch above the level of the umbilicus. It is not especially hard or sharp. There are no prominent veins over the abdomen.

The *eye-grounds* are somewhat pale, and the vessels look a little soft and flabby. There are no retinal hemorrhages.

The *urine* is pale, slightly turbid; specific gravity 1017; a small amount of albumin is present, and also a few granular casts. There is no sugar.

A blood examination the day after admission shows hæmoglobin, 58 per cent.; red cells, 2,500,000; white cells, 692,000.

DIFFERENTIAL COUNT OF 500 LEUKOCYTES.

Large and small mononuclears	8.0 per cent.
Transitional cells	2.0 "
Polynuclear eosinophiles	4.0 "
Polynuclear neutrophiles	37.5 "
Myelocytes, eosinophiles	3.5 "
Myelocytes, neutrophiles	45.0 "

In this count there were found several nucleated red cells, several mast cells, but no megaloblasts.

History after Admission. Second day: Severe attack of epistaxis. Ceased spontaneously. Slight diarrhœa. Sleeps badly.

Third day: Diarrhœa relieved by opium and bismuth.

Sixth day: Diarrhœa very troublesome again. Put on increasing doses of Fowler's solution.

Ninth day: Diarrhœa persists in spite of medication.

Thirteenth day: Hæmoglobin, 56 per cent.; red cells, 2,100,000; white cells, 620,000.

Fourteenth day: Pain in abdomen during urination. No hæmaturia. Has been voiding thirty-six to forty-six ounces daily. During next three days a marked diminution of urine. Returned to usual quantity under citrate of lithium.

Twenty-second day: Fowler's solution discontinued as patient begins to show physiological effects. Marked coryza. Hæmoglobin, 54 per cent.; red cells, 3,010,000; white cells, 208,000. The spleen is

considerably diminished in size. It is three inches below costal border, and seems softer. Liver also diminished in size.

Twenty-fourth day: Fowler's solution recommenced. Another attack of epistaxis.

Twenty-eighth day: Has had sore throat for several days. Throat congested, but no hemorrhagic areas. Now has severe pain in left ear, and slight deafness. No tenderness over mastoid. Arsenic again has to be stopped.

Thirty-first day: Still sleeps badly. Weight, 103 pounds. Spleen still smaller. Lower border only one inch below ribs. Liver also smaller. Apex beat of heart is now in fifth space. Drum membrane has ruptured, and there is a profuse bloody discharge from the left ear. Hæmoglobin, 60 per cent.; red cells, 2,971,000; white cells, 44,300.

Thirty-third day: Left ear drum punctured by Dr. Murray. This was followed for six days by such profuse bleeding that canal had to be tamponed. Puncture relieved pain, but deafness is steadily increasing. An organic iron preparation given.

Thirty-seventh day: Fowler's solution, gtt. xv, t. i. d., again begun.

Fortieth day: Has been constipated. Weight, 103½ pounds. Specific gravity of blood, 1041; hæmoglobin, 62 per cent.; red cells, 3,430,000; white cells, 22,000.

Forty-fifth day: Weight, 105¾ pounds. Spleen and liver still felt about one inch below ribs.

Fifty-second day: Weight, 109½ pounds. Fowler's solution increased 1 gtt. daily.

Fifty-ninth day: Hæmoglobin, 50 per cent.; red cells, 2,260,000; white cells, 54,000. Deafness increasing in both ears. Has been up about ward, but now returned to bed on account of weakness. Spleen a little larger. Is two inches below ribs, and liver three inches. Weight, 110 pounds.

Sixty-fourth day: Has been eating very little, and yesterday and to-day has vomited frequently. First elevation of temperature since admission. Highest is 102° at 8 P.M. Next day 102.4° in evening. Evening temperature continued like this until death.

Sixty-fifth day: General abdominal pain for first time. No tenderness.

Sixty-eighth day: Diarrhœa again troublesome. Fowler's reduced to gtt. xviii, t. i. d.

Seventieth day: *x*-ray over spleen for eight minutes; five ampères; distance, nine inches. Diarrhœa checked with opium.

Seventy-second day: *x*-ray over spleen for twelve minutes; six ampères; distance six inches.

Seventy-third day: Fowler's solution reduced to gtt. x, t. i. d. Strychnine, gr. $\frac{1}{40}$, every four hours. *x*-ray to spleen for nine minutes; five ampères; distance seven inches.

DIFFERENTIAL COUNT OF 500 LEUKOCYTES.

Large and small mononuclears	9.0 per cent.
Transitional cells	5.0 "
Polynuclear eosinophiles	0.5 "
Polynuclear neutrophiles	22 0 "
Myelocytes, eosinophiles	0 5 "
Myelocytes, neutrophiles	63.0 "

During this count one megaloblast, seven normoblasts, and a few poikilocytes were found. Myelocytes are not uniform in size, many being much smaller than at the first count. Many of their nuclei stain faintly and show signs of degeneration. A few mast-cells present.

Seventy-fourth day: Eyelids reddened and complains of photophobia. Deafness is now complete. Complains of severe pains over liver and spleen, and attributes this to the *x*-ray. Patient says he can "feel the *x*-ray working" during treatment. *x*-ray discontinued on account of patient's weakness, which is progressing rapidly.

Hæmoglobin, 32 per cent.; red cells, 1,920,000; white cells, 7000 (!). (Count verified).

Seventy-fifth day: Very restless; complains of severe abdominal pain. Respirations very labored. Dulness, harsh breathing, and moist rales over both lungs behind. Coma about noon, and death at 6.30 P.M.

Autopsy Fifteen Hours after Death. Rigor mortis slight; post-mortem lividity in dependent parts. Emaciation marked. Abdomen prominent.

Left Lung. Pleural cavity dry. A few slight adhesions at base. Deposits of coal-dust on parietal pleura. Lung weighs twenty-seven ounces. Crepitant all over except at base, where there is considerable hypostatic congestion. There is a marked general anthracosis. No tubercular scars.

Right Lung. Pleural cavity dry. There are a few slight adhesions at both apex and base. Anthracotic deposits on parietal pleura. Lung weighs thirty-one ounces. Pleura at apex is slightly contracted, but there are no definite signs of tuberculosis in the lung substance. Hypostatic congestion at base, but less marked than on left side. Same condition of anthracosis.

The *bronchial glands* and the glands around the lower part of the trachea are markedly anthracotic.

Heart. Pericardium is normal. Contains about one ounce of clear fluid. Heart weighs ten ounces. Muscle tissue pale. A small chicken-fat clot in left ventricle. Aortic and mitral valves are normal. No atheroma of arch of aorta. Papillary muscle pale. No zebra stripes. Ventricular wall of normal thickness. Chicken-fat clot in left ventricle. Pulmonic and tricuspid valves normal.

Spleen. Very dense adhesions to diaphragmatic peritoneum and to intestines. Weight, 52 ounces. Longest diameter, 21 cm. The

cut surface is very firm, dark-red connective tissue, trabeculæ stand out prominently; the Malpighian bodies are not distinct. There is an old infarct at the upper pole, two inches in diameter on the surface; it is evidently undergoing fatty changes. The splenic pulp surrounding this infarct is markedly hemorrhagic. There are also numerous hemorrhagic spots in other portions of the spleen. In the lower part of the organ there are two other smaller infarcts.

Liver. Weight, 77 ounces. Color pale and waxy-looking. There is slight retraction of the cut edges of the capsule. Moderate degree of chronic congestion.

The general *peritoneum* is normal. Foramen of Winslow patent. The gall-bladder, urinary bladder, and pancreas are normal. There are several anthracotic glands around the head of the pancreas. There are no anthracotic glands in the lesser omentum. The mesenteric and retroperitoneal glands are not enlarged.

Alimentary Canal. There is marked chronic congestion of the mucous coat of the stomach, with considerable post-mortem digestion. There is also a marked congestion of the upper half of the small intestine. Large intestine is normal. Appendix normal, directed down and in toward pelvis. No trace of Meckel's diverticulum. No intestinal parasites.

Kidneys. Both similar. Weight, 5 ounces each. Capsule strips easily. Cut surface is rather pale. Cortex of normal thickness, and markings fairly distinct.

Prostate of normal size.

The *bone-marrow* of the ribs is dark red and does not present other unusual features. The marrow of the humerus is deep red, firm, and stands out prominently from the broken ends.

Microscopic Examination. (Tissues fixed in formalin and alcohol.)

Liver. There is some slight increase in the connective tissue. The liver parenchyma cells are fairly normal. They do not show fatty degeneration. The frequently described deposits of white blood cells are numerous. They are most prominent around the central veins and seem to consist principally of mononuclear cells and myelocytes. The central veins are generally empty, but many of the smaller arterioles seem to be plugged with leukocytes. There are a few small areas of extravasated blood among the liver cells in which the leukocytes are numerous. The capillaries of the liver are not dilated.

Lungs. These show the usual changes from anthracosis which are common in those who have worked a long time in coal mines. There is a considerable deposit of coal-dust in the walls of the air vesicles, in the connective-tissue septa, under the pleura, and around the bronchi and bloodvessels. There is some thickening of the walls of the air vesicles, and there is an increase of connective tissue around the larger deposits of dust. There is but little

swelling and desquamation of epithelial cells, as is sometimes seen in those who have worked in the mines up to a few days of their death. There is no sign of a tubercular inflammation. The alveolar capillaries are not distended. At the bases of the lungs there is the ordinary picture of hypostatic congestion. In some places where there is an increase of connective tissue due to the anthracosis there are large deposits of leukocytes.

Heart Muscle. This shows quite a marked degree of fibrous myocarditis. The muscle cells are separated in many places by large patches of fine, poorly staining fibrillar connective tissue, with a few spindle-shaped nuclei. There are no deposits of white cells in the sections examined.

Pancreas. Normal.

Kidneys. These are but little changed. No special increase in the connective tissue. The glomeruli are normal. There is some swelling and cloudiness of the cells of the secreting tubules. No deposits of leukocytes are seen.

Alimentary Canal. Sections from the portions of the stomach saved show but little mucous membrane. The subserous and muscular coats are normal. Sections from the small intestine are normal.

Lymph Glands. The only glands preserved for cutting were those around the trachea. In these the deposit of coal-dust is so great that the fine structure is entirely obscured.

Spleen. (Stains by eosin and Delafield's hæmatoxylin, picro-acid fuchsin, carmine, borax, eosin, and methylene blue.) Sections from the infarct show no splenic tissue, but only dense fibrous connective tissue, with a few poorly formed bloodvessels. Surrounding the infarct in the splenic tissue there is a diffuse infiltration of old, much degenerated, blood. Throughout the splenic tissue proper the most marked change is an enormous increase in the normal connective tissue. This is represented both by an increase in size of the trabeculæ and by an increase in the intercellular reticulum. The Malpighian bodies are nowhere well formed and prominent. Throughout the splenic pulp there is a considerable infiltration of blood cells, which are in some places much degenerated; in others they are comparatively fresh. In the pulp the predominating cell is, of course, the small round lymphoid cell. In the blood cells extravasated in the splenic pulp there are a larger number of normoblasts and also more megaloblasts apparently than were seen in the smears during life. There are also many cells resembling the myelocytes, but considerably changed by the hardening process. A few of these latter show distinct mytotic figures. This was not noted in the blood during life. In a prolonged examination of the sections one polynuclear eosinophile leukocyte was seen. As usual in miners, there are many fine coal-dust particles scattered diffusely throughout the intercellular spaces of the spleen.

Bone-marrow. Smears from the ribs and humerus taken at the autopsy and stained by the blood methods show the same elements as the circulating blood, except that the normoblasts and megaloblasts are much more numerous. There are a few eosinophiles. Pieces of the ribs and humerus were decalcified in 5 per cent. nitric acid, hardened in alcohol, and stained by the same methods as the spleen. These sections show more marked changes from the normal than any other tissue examined. There are no fat or large "marrow" cells, and the whole appearance closely resembles that of well-formed granulation tissue. There is a fine connective-tissue reticulum, in the meshes of which there are cells which vary much in morphology and staining properties. Most of these cells are round and somewhat larger than a red cell. Their protoplasm is homogeneous, and takes the eosin faintly. They have a quite small, round, homogeneous nucleus. There is another, less frequent type of cell, which is larger, oval, granular, stains deeply with eosin, and has a large granular oval nucleus. There are a few very large cells resembling myelocytes, but it is difficult to trace much resemblance between the cells previously found in the circulating blood and those in the marrow sections after treatment by nitric acid and alcohol.

The Blood Picture. There is little to note in the red cells. They stain well; there is no polychromatophilia. Poikylocytes and normoblasts were noted, especially toward the last of the disease, and were not very numerous at any time. Megaloblasts were also present in small numbers. These were about three times the size of an ordinary red cell, and, while the nucleus was sometimes irregular, none showed definite mitosis.

The myelocytes which predominated were quite characteristic in type. As the total number of leukocytes diminished the morphology of these cells also changed. Many were much reduced in size, the nuclei stained faintly, and the granules became less prominent. The eosinophile myelocytes were also characteristic. These gradually fell in number from 3.5 per cent. to 0.5 per cent. of all leukocytes. And in the last slide examined none were found. The polynuclear eosinophile leukocytes, which at first showed a relative increase, also diminished, and finally disappeared as the disease progressed to its termination.

The accompanying chart graphically shows the course of the blood changes as determined by weekly counts.

Among the points of interest in this case are:

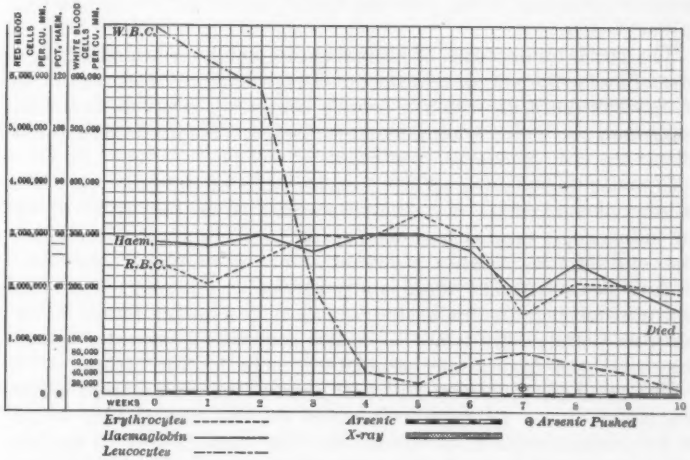
1. The fact that the man performed the active duties of an inside mine foreman for certainly two and probably six years after his disease began, and that he continued work up to ten weeks before the fatal termination.

2. The high leukocyte count of 692,000. We have not made an exhaustive search of the literature on this point, but among some

forty recent cases in easily available journals there was not given a higher count in chronic cases. An acute case of Hamman[1] and another quoted by him gave 958,000 and 790,000, respectively. While in exceptional cases the white may equal or exceed the red cells, our proportion of 1 : 3.6 is much above the average.

3. The disappearance of the previously increased eosinophiles. This fact, taken with Simon's case noted below, would tend to show that an increase in the number of eosinophiles is not so important a feature of this disease as has been considered.

4. An interesting symptom in this case was the deafness, which began in the fourth week of his stay in the hospital, and finally became complete. Deafness, while mentioned as a symptom in text-books—*e. g.*, Osler—is not spoken of in any case we have



reviewed, except that of Mott.[2] Mott attributed its presence in his case to hemorrhage into the middle ear. That this is the true cause is well demonstrated in our case, as a hemorrhage actually did occur and spontaneously perforated the membrane. Bleeding was profuse for several days.

5. The great prominence of intestinal symptoms throughout the disease, suggesting autointoxication from the intestinal tract as a possible cause.

The most interesting questions arising in the study of leukæmia are connected with its etiology and with the relation of the different forms to each other.

During the last few years the infectious theory of its origin seems to be rapidly gaining ground. The acute leukæmias certainly seem to be infectious in origin, and the frequency of pharyngeal and

tonsillar inflammation as a mode of onset cannot be ignored. The acute form of the disease, aside from its origin, frequently shows a decidedly septic type. Fussell, Jopson, and Taylor[3] noted this in thirty-one out of fifty-six acute cases which they collected.

Vehsemeyer placed leukæmias among autointoxications from the intestinal tract. As noted above, our own case suggests this, as diarrhœa was a prominent symptom throughout, especially at each exacerbation of the disease. During one of these, while under Dr. Thompson's care, he improved under small doses of calomel continued daily. Some of the exacerbations seem to have been relieved simply by a selected diet.

Simon's[4] case had recurring attacks of dysentery for twelve years before the apparent onset of the leukæmia. Diarrhœa was also a marked symptom in the previous history of Jewett's[5] case and of Miller's[6] case.

The much-quoted case of Obrastow, in which an attendant on a case of leukæmia also developed the disease in a few weeks, and one of Jewett's cases, in which a brother and sister seem to have had leukæmia, also point to an infectious disease. These cases in themselves are not, of course, conclusive.

Chmelar[7] fairly sums up the present status of the question when he says of leukæmia: "It has no specific cause, but arises under the influence of various acute and chronic infectious diseases, which alter and lead to excessive proliferation of the lymphoid elements." It does not seem that there is any connection between leukæmia and coal-mining, as this is the only case in a miner found in the last five years in the board of health records of Scranton, which has the largest coal-mining population in the United States.

The trend of opinion on the other point of the disease most under discussion—*i. e.*, the relation between the different clinical forms of leukæmia—seems to be toward the view that there is no specific difference between lymphatic and myelogenous leukæmia, but that they both are closely allied forms of fundamentally the same pathological condition. It would seem that the former sharp differentiation from the blood picture alone is little more than symptomatological. Indeed, if the hæmatologists are to make the classifications they will have to assume another form to include Simon's case of the myelogenous type without eosinophile cells. It would, perhaps, be as logical to consider tuberculous peritonitis with serous diffusion a specifically different morbid entity from the same disease with fibrin and adhesions.

The evidence as to fundamental unity of the two forms has now become a fairly logical chain, and is well summed up by Reed.[8] There seems little doubt now but that the acute and chronic forms are different only in the clinical course. While the acute type is generally the lymphatic, the myelogenous form does occur, as shown by the cases of Hirschfield and Cabot.

The first step in the evidence of the real identity of the two forms came in 1870 from Neuman. He showed that in each form the changes in the bone-marrow are marked. Reed's case, among others, seems, as she says, "to prove conclusively that we have here a lymphocytosis arising from proliferation of cells in the bone-marrow, and death occurring before any other organs showed involvement."

The establishment, too, of a mixed form of the disease further tends to show the close fundamental relation between the forms of leukæmia, and it seems that we will ultimately have to accept Reed's conclusion that "there are three forms of leukæmia, all due to myelogenous changes, and that they should be known as myelocytic, lymphoid, and mixed varieties, if we wish to make the blood picture the basis for clinical divisions."

The treatment of the disease is also an interesting feature. The value of arsenic, while real, is seldom more than temporary, though Simon and Campbell[9] report one case in which for a year the splenic tumor has been absent and the number of leukocytes normal. The authors believe that this is the only case on record showing this long-continued improvement. In our own case, as stated above, the disease was apparently held in check for probably six years by courses of arsenic.

The *x*-ray treatment is very promising, but its permanence cannot at this date be said to be proven. Heinke's[10] experimental work seems to show that the rays have a definite selective action, causing changes of a retrograde character in the spleen and lymphatic glands. From our present idea of the disease, however, this would apparently be attacking only a secondary result. Its curative action on the bone-marrow has yet to be demonstrated.

In our own case nothing can be inferred from the marked fall in leukocytes shortly after commencing the use of the rays, as the change may have been an ante-mortem one.

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ON TWO CASES OF WEIL'S DISEASE COMPLICATED BY THE TEMPORARY APPEARANCE OF SMALL TUMORS IN THE LIVER.

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Small palpable tumors of the liver are found in malignant neoplasms, and more rarely as a result of gummatous changes of this organ. The first end fatally, the latter may be cured by long-continued antisyphilitic treatment; without these measures the latter are also permanent.

A temporary occurrence of tumors in the liver, which disappear again in the course of a few days, has not been mentioned in literature as far as I know. I have, however, observed two such cases, and believe that it would be of interest to describe them here somewhat minutely and to add some remarks.

Case I (*December* 1, 1903). —August R., aged sixty-seven years, has been suffering for many years from his stomach and bowels. His appetite used to be fickle, and he was occasionally troubled with diarrhœa. During the last two or three years the patient was much better; he could eat better, felt stronger, and had a regular action of the bowels. The present trouble began three or four days ago. The patient felt weak, his appetite disappeared, the bowels were constipated, and severe headache was present.

Status Præsens. Pulse, 110; temperature, 101° in the mouth. In the thorax below and behind there are a few dry and moist rales. The hepatic dulness begins in the right mammillary line at the lower margin of the fifth rib, and extends one to two fingers' breadth below the costal margin. By means of palpation two protuberances of walnut size are distinguished in the right lobe of the liver; the liver and these tumors feel harder than normal. The left lobe of the liver is also swollen and sensitive, but does not exhibit any tumors. The spleen is enlarged.

The urine, of a specific gravity of 1023, shows the presence of albumin and casts.

Patient received 15 grains of calomel and was placed upon a strictly liquid diet.

December 2d. Temperature fluctuates between 103° and 104°. Urine contains some bile pigment and a great deal of albumin, no sugar; the diazo reaction is positive; Widal negative.

The patient complains of headache, cough, and weakness. The nervous system is perfectly free. The skin and scleræ are jaundiced, otherwise the condition is the same. Patient is given liquor ammon. anis., and heroin.

Since December 5th the temperature curve ran lower, and on the 8th returned to normal. The liver now shows no tumors, and is less swollen; the urine is free from bile and albumin. The cough disappeared and patient began to feel better and stronger. About fourteen days later the patient was perfectly well.

CASE II. (*April* 26, 1903).—Frederick S., aged about fifty years, was taken sick three days ago with vomiting and diarrhœa, loss of strength, insomnia, and fever. There was absolute anorexia and constant nausea, with frequent vomiting.

When I examined the patient I found a pulse of 100, temperature 102°. His face was flushed, tongue strongly coated; speech indistinct and stuttering; slight tremor in the hands. Color of skin and scleræ is slightly icteric. The abdomen is somewhat distended, the epigastric region markedly sensitive to pressure. The hepatic dulness begins in the right mammillary line at the upper margin of the sixth rib and extends two to three fingers' breadth below the costal margin. The consistency of the liver is harder than normal. On the convex surface of the right lobe there are three hard tumors of the size of a walnut, which can be easily palpated and are sensitive to pressure.

The splenic dulness is considerably enlarged, but the organ cannot be palpated. The urine is strongly concentrated, contains much sugar, albumin, and casts; diazo reaction is strong, and traces of bile are present. The patient complains of severe abdominal pains, vomiting, bad taste in the mouth, and insomnia, as well as of a harassing dry cough. He was given sodium bicarbonate and codein; liquid diet, veronal.

April 27th. Patient has slept, with interruptions; complains of a severe diarrhœa; says the stools smell very fetid. His condition is about the same as on April 26th. Widal reaction and malarial plasmodia are not found. He is ordered codein and tannigen.

30th. Fever is still present, but shows larger remissions. General condition is somewhat better. Objectively we still have the same symptoms of spleen and liver swelling; the urine contains albumin and sugar, but no bile. The diarrhœa has disappeared, vomiting and nausea no longer exist, and the patient can take nourishment better; he has a clear mind and speaks naturally.

May 2d. Temperature reaches only to 100.4°, pulse being 76; the nodes on the surface of the liver are less prominent and not so easily palpated; the liver is less swollen and less sensitive to pressure. Spleen is also smaller, the urine contains no sugar, shows no diazo reaction, but still traces of albumin.

5th. Temperature is normal; the liver projects only a finger's width over the margin of the ribs; the nodes cannot be palpated. The color of the skin is clearer, the splenic enlargement has disappeared, and the patient feels better in general, but is still quite weak. The urine is free from sugar and albumin. He began to

be up and about now daily and to take more food. In the course of five to six weeks the patient was completely well.

Epicritic Remarks. Both cases show a marked resemblance in their main features. In both the disease began, after a short prodromal stage, with fever, severe gastric disturbances, and general weakness. During the period of fever which lasted about a week, a marked enlargement of spleen was found as well as of the liver. Albumin was present in the urine, as well as a diazo reaction, and a trace of bile pigment in both, whereas sugar was found only in one case. Both had bronchitis. Cerebral symptoms, insomnia, severe headache, and disturbances of speech (some stuttering) were present in one case but not in the other. Widal's test was negative in both cases, and plasmodia were not found in the blood. After about a week's illness convalescence takes place. The fever and the albumin in the urine disappear; the gastric disturbances abate, and the swelling of the spleen and liver decreases, so that in the course of a few days these organs appear perfectly normal. There remains a condition of weakness which, however, disappears in the course of a few weeks, and the patients are then perfectly well. What is most remarkable in these cases is the fact that during the height of the disease small hard tumors appear on the hepatic surface which again entirely disappear with the abatement of the fever.

The clinical picture of these cases corresponds in the main to the symptom-complex described by Weil,[1] differing, however, from it by the transient formation of nodes of walnut size on the surface of the liver. With regard to the origin of the latter we may assume that this process in the liver is analogous to that of the acute nephritis existing in these cases (as evidenced by the albumin and casts in the urine). In other words, we probably have to deal here with an acute hepatitis with particularly prominent, severely affected, circumscribed foci. These nodes may be caused by an accumulation of exudative products, which again disappear with the subsidence of the inflammation.

Hepatitis resulting in a cure is often encountered. Budd[2] published some observations on this point which were later confirmed by Frerichs.[3] In Budd's book I find the following: "There are probably various morbid states of the secreting substance of the liver in which, as in erysipelas of the face and in the affections of the joints in rheumatic fever, the fluids poured out during the inflammatory process become again absorbed, leaving no permanent traces or only such traces as cannot be well distinguished. In such cases the nature of the morbid process can be judged of by

[1] A. Weil. Ueber eine eigenthümliche mit Miltztumor, Icterus und Nephritis einhergehende acute Infectionskrankheit., Deutsches Arch. f. klin. Med., 1886, Bd. xxxix. p. 209.

[2] George Budd. Diseases of the Liver, 1857, p. 167.

[3] Frerichs. Krankheiten der Leber, vol. i.

the symptoms only, unless the patient happened to die during the acute state of the malady and while its effects are still present."

Further on he says: "I have met with several instances in which enlargement of the liver has come on, and more than one in which jaundice has come on, soon after the disappearance of the rash and scarlatina; but I have never had an opportunity of inspecting the liver in a case of this kind. It is most probable that the disease of the liver is analogous to the disease of the kidney which so often occurs in scarlatina after the disappearance of the rash, and that the enlargement of the liver results from rapid development and shedding of the secreting cells caused by the elimination of some noxious matter through the gland."

The occurrence of palpable tumors (of about the size of a walnut) of the liver, which again disappear with the inflammation, is, however, not mentioned either by Budd or by Frerichs. Nevertheless, I believe that we have to deal here with a similar process.

The fact that distinctly palpable tumors of the liver may occur, existing only a few days in order to disappear again, must be of interest in a high degree, the more so as they cannot be differentiated by palpation from malignant or gummatous tumors. If, therefore, we meet such tumors in a patient suffering from fever, it is best to wait with the diagnosis of cancer or gumma of the liver until further observation permits a definite diagnosis.

VOLUMETRIC DETERMINATION OF THE PURIN BODIES (URIC ACID AND THE PURIN BASES) IN URINE.[1]

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and

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The object of this paper is to describe an exact and clinical method of determining the uric acid and the purin bases in the urine. A great many methods have been devised for this purpose, the simpler ones being, as a rule, inaccurate, and the more exact ones of a complex nature requiring a great deal of time and a degree of technical skill not possessed by the average practitioner of medicine.

All the more exact methods are founded upon the property of uric acid and the purin bases of forming definite compounds with silver in an ammoniacal solution of the latter in the presence of

[1] Read before the New York County Medical Society, March 28, 1904.

neutral salts of the alkaline and alkaline earth group, preferably chloride of magnesium, chloride of lithium, or chloride of ammonium. Under the above conditions uric acid combines with silver in the proportion of one molecule of the former and one atom of the latter; the purin bases in the proportion of two molecules of xanthin to one of silver. The compound of silver urate formed under the above conditions is, as we shall show later, insoluble in both weak and strong ammonia up to 1: 200,000 parts. The compounds of silver and purin bases are soluble in strong ammonia, insoluble in weak ammonia.

In the standard method of Ludwig-Salkowski the procedure is as follows: A known quantity of urine is precipitated by a solution of silver in an ammoniacal magnesium mixture; the precipitate after being carefully washed out is decomposed by sodium sulphide, which separates the silver from the uric acid and purin bases as an insoluble sulphide of silver and dissolves the purin bodies. This solution is treated with weak hydrochloric acid, thus separating the uric acid, which crystallizes out after twenty-four hours, leaving the purin bases in solution. The uric acid is then weighed.

For the determination of the purin bases the solution that has been filtered off from the uric acid is treated with an ammoniacal solution of silver, which precipitates the purin bases as purin silver. After washing out this precipitate the silver is determined either by the method of Vohlhard or by ignition and weighing the residue, and thus the amount of the purin bases is determined.

We have omitted to describe all the necessary precautions in this analysis, but one can well imagine what a tedious and long process it is, and, as will be shown later by our experiments, some grave errors are scarcely to be avoided.

Another method of analysis, in view of the facts already mentioned (that the compounds of the purin bodies with silver are definite), is to determine the silver in the precipitate. This method —Haycraft's—is a fairly good one, but, as Huppert says, requires a great deal of skill and precision.

Instead of determining the silver in the precipitate the attempt has been made by Denigès and Czapek to proceed, as above mentioned, with a known amount of silver and to determine the excess of silver in an aliquot part of the filtrate. Denigès used potassium cyanide and Czapek used potassium sulphide. In both methods, and especially the latter, the solution used for titration is unstable and the titre requires to be verified very often. In addition, in the methods of Haycraft, Denigès, and Czapek, the total amount of purin bodies is determined. For the determination of uric acid these methods are not applicable.

Our method is also founded upon the titration of the excess of silver added. It differs from that of Denigès and Czapek in the following respects: For titration we use a solution of potassium

iodide, the titre of which is unchangeable; and, secondly, having by experiments found that silver urate in strong ammonia solutions is insoluble, and that the silver compounds which the purin bases form in the same menstruum are soluble, we are enabled to determine both these bodies by the same procedure.

REQUIREMENTS.

(1) $\frac{N}{50}$ Ag solution.

(2) $\frac{N}{50}$ KI solution.

(3) A nitrous-sulphuric acid mixture.

(4) Starch solution.

(5) NH_4OH. Sp. gr. 0.90.

1 c.c. $\frac{N}{50}$ Ag solution = 0.00336 gr. uric acid = 0.00152 gr. purin base, calculated as xanthin.

The $\frac{N}{50}$ Ag solution is prepared by dissolving 3.3932 grms. $AgNO_3$ previously heated to 120° C. for ten minutes in water, adding 75 c.c. NH_4OH (sp. gr. 0.90) and 10 grms. NH_4Cl and diluting to 1 L. Crystals of pure $AgNO_3$ can be obtained in the market.

The $\frac{N}{50}$ KI solution is prepared by dissolving 3.3200 grms. KI previously heated to 180° C. in water and diluting to 1 L. KI free from iodate, chlorides, and sulphate can be readily obtained.

The nitrous-sulphuric acid mixture is prepared by adding 25 c.c. concentrated H_2SO_4 to 75 c.c. of H_2O and then adding 1 c.c fuming nitric acid.

The $\frac{N}{50}$ solutions are stable, the titre remaining constant after several months, provided the ordinary precautions in preserving silver solutions are observed.

METHOD. *To Determine Uric Acid.* To 110 c.c. of urine add 55 c.c. $\frac{N}{50}$ Ag solution and dilute with NH_4OH (sp. gr. 0.90) to 220 c.c. All these measurements can be conveniently made in flasks of the Giles pattern. Mix and filter through a dry folded filter, either at once or after standing a few minutes. Two portions of 100 c.c., each of which corresponds to 50 c.c. of urine, are collected.

In the mean time a half-dozen small test-tubes (about 8 cm. long and 1 cm. in diameter) are filled for about 1 cm. with a mixture of, roughly, two parts of the nitrous-sulphuric acid and one part starch solution.

To one of the above portions of 100 c.c., $\frac{N}{50}$ KI is rapidly added, and after each addition of 2 c.c. a small portion, not exceeding 0.5 c.c., is removed by means of a pipette, which also answers as a

stirring rod, and carefully introduced down the side of one of the test-tubes in such a manner that two absolutely distinct layers are formed. The end reaction manifests itself sharply by the formation of a blue ring (iodide of starch) at the point of juncture. Having now found the end point approximately with the first 100 c.c., the exact end point is determined with the second 100 c.c.—*e. g.*, say that more than 10 c.c. and less than 12 c.c. are required with the first 100 c.c. The second 100 c.c. are then taken, and 10 c.c. $\frac{N}{50}$ KI run into the solution at once; then a few drops at a time are carefully added, until the exact end point is reached. With a little practice the exact end point can be obtained without having removed more than 1 c.c. from the solution being tested. The entire analysis need not require more than from twenty to twenty-five minutes.

To Determine the Purin Bases. Exactly the same process is carried out except that instead of adding strong NH_4OH we dilute with water—*i. e.*, take 110 c.c. of urine, add 55 c.c. $\frac{N}{50}$ Ag and dilute with water to 220 c.c. and proceed as before. The number of c.c. of $\frac{N}{50}$ Ag used equals the total purin bodies, and, subtracting the number of c.c. of $\frac{N}{50}$ Ag required in the uric acid determination, the difference equals the purin bases. For example:

Determination of Uric Acid.

110 c.c. urine taken; 55 c.c. $\frac{N}{50}$ Ag added; 55 c.c. NH_4OH 0.90 added; 220 c.c. final dilution.

100 c.c. filtrate = 50 c.c. urine = 15.9 c.c. $\frac{N}{50}$ KI less 0.3 c.c. correction;

$$25.0\ \frac{N}{50}\ \text{Ag added} - 15.6 = 9.4\ \frac{N}{50}\ \text{Ag used.}$$

$9.4 \times 0.00336 = 0.0316$ grm. uric acid in 50 c.c. urine, from which the amount in twenty-four hours is calculated.

Determination of Purin Bases.

110 c.c. urine taken; 55 c.c. $\frac{N}{50}$ Ag added; 55 c.c. water added; 220 c.c. final dilution.

100 c.c. filtrate = 50 c.c. urine = 14.2 c.c. $\frac{N}{50}$ KI less 0.3 c.c. correction = 13.9 c.c.

This 100 c.c. contained 25 $\frac{N}{50}$ Ag added; 11.1 $\frac{N}{50}$ Ag used less 9.4 uric acid Ag = 1.7 purin bases Ag.

$0.00152 \times 1.7 = 0.0026$ grm. xanthin in 50 c.c. urine, from which the amount in twenty-four hours is calculated.

PRECAUTIONS NECESSARY. 1. It is necessary in making the test for iodine that the solutions should be absolutely cold, and it is preferable to place the test-tubes in ice-water.

2. The end reaction can be best observed most accurately in daylight.

3. Many urines, if added to the nitrous-sulphuric acid mixture

and tested by the contact method will develop a reddish-colored ring at the point of contact. This color is due to the action of the acid on the coloring matter of urine, and must not be confounded with the distinctly blue ring produced when iodine is present. The reddish ring becomes apparent only when working with the weak ammoniacal solution, for in the strong ammoniacal solution the AgI precipitates more rapidly, is of a white color and not yellowish, and consequently sets off the blue ring by contrast. If doubt exists as to the nature of the ring it is only necessary to gently shake the test-tube without causing the liquids to mix completely; under these conditions the reddish ring becomes entirely dissipated, whereas the blue iodine ring becomes more distinct.

4. If the relationship of the standard solutions is determined under the same conditions as those under which the analyses with urine are carried out, it will be found that 0.3 c.c. more of the $\frac{N}{50}$ KI will be required to develop the end reaction than the number of c.c. of $\frac{N}{50}$ Ag used. This is owing to the fact that there is a limit to the delicacy of the test for iodine, and that it is necessary to add 0.2 c.c. $\frac{N}{50}$ KI to 100 c.c. H_2O in order that 0.5 c.c. of this dilution should give the reaction for I. When we remember that this 0.5 c.c. contains only 0.00332 mgr. of KI the extreme delicacy of the end reaction as performed by the contact method is appreciated.

Rogovin[1] has recently shown that the $HNO_2 + H_2SO_4$ test is the most delicate test for I. We came to this same conclusion independently, but found that by the contact method we could increase the delicacy of the reaction to a marked degree. The $\frac{N}{50}$ Ag and $\frac{N}{50}$ KI should therefore be standardized, using approximately the same dilution (100 c.c.) as in the analysis of urine, and the necessary correction obtained, which will be 0.3 to 0.4 c.c. if the solutions have been accurately prepared.

In order to prove the accuracy of our method in determining both uric acid and the total purin bodies, the following points were established experimentally:

1. That the Ag compound formed with uric acid under the conditions stated is insoluble both in dilute and in strong NH_4OH solutions.

2. That the Ag compound formed with the purin bases under the conditions stated is insoluble in weak ammoniacal solution and soluble in strong NH_4OH.

3. That known amounts of uric acid, when added either to water alone or to urine, can be accurately determined. This was shown

[1] Berliner klin. Wochenschr., 1903, S. 863.

to be the case under varying conditions and with uric acid from various sources.

4. That the uric acid determinations agree with determinations made by the Ludwig-Salkowski method.

5. That the determinations of the total purin bodies agrees with the results obtained by Arnstein's modification of Camerer's method.

6. That Ag can be determined with great accuracy by means of KI in an ammoniacal solution.

We shall in a separate paper publish a comparison of the accuracy of this means of determining silver as compared with other volumetric methods.

EXPERIMENTAL PART. (1) *With Uric Acid.* The uric acid which was used was obtained from three sources: two were commercial products and one was obtained from urine. The purity of one of the commercial products (A) was established by nitrogen (Kjehldal) determinations, as follows:

	Per cent.	
	Found.	Calculated.
0.0814 gr. yielded 0.0269 gr. N	33.06	33.33
0.0952 gr. yielded 0.0316 gr. N	33.20	

The second commercial product (B) was purified by recrystallization and the uric acid from urine (C) was purified by washing with alcohol and repeatedly recrystallizing till an almost colorless product was eventually obtained.

Solubility of the Precipitate which Uric Acid Forms with an Ammoniacal Solution of Silver Containing Ammonium Chloride. 0.100 gr. of uric acid (A) was dissolved in 10 c.c. of a cold saturated solution of $LiCO_3$ and diluted to 100 c.c. This solution is designated "D." The solubility was determined both in water and in urine. A urine free from all purin bodies was prepared by precipitating these bodies by means of Salkowski's ammoniacal silver solution and then adding only enough NH_4OH to dissolve the AgCl formed. In each case the final dilution was 50 c.c., and this contained 2 c.c. of the $\frac{N}{50}$ Ag solution.

Solubility in Water.

Solution "D" added . .	1.00 c.c.	0.5 c.c.	0.25 c.c.
Uric acid	1.00 mg.	0.5 mg.	0.25 mg.
Corresponding to 1 part in	50,000	100,000	200,000
Result	Marked precipitate.	Slight precipitate.	Very slight precipitate, readily noticeable on standing eighteen hours.
	Containing 25 per cent. NH_4OH.		Sp. gr. 0.90.
Solution "D" added . .	1.00 c.c.	0.5 c.c.	0.3 c.c.
Uric acid	1.00 mg.	0.5 mg.	0.3 mg.
Corresponding to 1 part in	50,000	100,000	167,000
Result	Slight precipitate.	Very slight precipitate which collects after eighteen hours.	Turbidity which settles as a precipitate after eighteen hours.

Solubility in a Purin-free Urine.

Solution "D" added . .	1.0 c.c.	0.5 c.c.	0.25 c.c.
Uric acid in	1.0 mg.	0.5 mg.	0.25 mg.
Corresponding to 1 part in	50,000	100,000	200,000
Result	Marked precipitate.	Precipitate.	Slight precipitate.
	Containing 25 per cent. NH_4OH.		Sp. gr. 0.90.
Solution "A" added . .	1.0 c.c.	0.5 c.c.	0.25 c.c.
Uric acid in	1.0 mg.	0.5 mg.	0.25 mg.
Corresponding to 1 part in	50,000	100,000	200,000
Result	Precipitate.	Slight precipitate.	Turbidity which settles as a precipitate in eighteen hours.

The results show that in urine, whether in a weak or strong ammoniacal solution, the silver urate precipitate is less soluble than 1 part in 200,000; or, in other words, so slight as to be negligible. The same is practically true of aqueous solutions.

Solubility of the Silver Precipitate Formed by the Purin Bases in NH_4OH in the Presence of Urine. The purin bases were separated from 1000 c.c. of urine according to the method of Salkowski.[1] The acid solution (E) containing these bases, which probably also contained a trace of uric acid, was diluted to 100 c.c.

A urine from which all the purin bodies had been removed was used in making the following tests:

Twenty c.c. of solution E containing the purin bases were added to 200 c.c. of the purin-free urine (F). A small quantity of $\frac{N}{50}$ Ag solution was then added and a voluminous precipitate obtained. The same experiment was repeated, except that enough NH_4OH of specific gravity 0.90 was added to form 25 per cent. of the final dilution. Under these conditions instead of a voluminous precipitate being formed, only a slight turbidity was produced, thus proving that the purin bases are practically entirely held in solution in an NH_4OH solution of this strength, and are perhaps entirely soluble, since the turbidity obtained was in all probabliity caused by the trace of uric acid which the solution used contained.

In the presence of solutions containing less than 25 per cent. NH_4OH, the purin bases are progressively less soluble. The same results have been obtained in control experiments. Moreover, it is a fact that although the precipitate of the Ag compound can readily be prevented if sufficient NH_4OH be present, it is much more difficult to dissolve this precipitate if once formed in a weak NH_4OH solution, even though strong NH_4OH is then added in large excess.

Determination of Uric Acid in Aqueous Solutions. In the following experiments the commercial uric acids "A" and "B" and

[1] Pflüger's Archiv, 1898, Bd. lxix. p. 280.

the uric acid from urine "C" were used as indicated. As a rule, the uric acid was dissolved in 15 to 20 c.c. of a saturated solution of $LiCO_3$ in the cold. In a few instances Na_2CO_3 was used, in which cases the solution was slightly warmed.

Fifty-five c.c. $\frac{N}{50}$ Ag were invariably added. In some cases which are indicated the precipitation was made in the presence of 55 c.c. NH_4OH, specific gravity 0.90. The final dilution was always 220 c.c., and the determinations were made in two portions of 100 c.c. each.

Number of experiment.	Source of uric acid used.	Total uric acid dissolved.	Solvent used.	$\frac{N}{50}$ Ag required for 100 c.c.	Uric acid found.	Uric acid added.
1	A	0.1133 gr.	$LiCO_3$	15.3 c.c.	0.0514 gr.	0.0515 gr.
2	A	0.1110 "	"	14.8 "	0.0497 "	0.0505 "
3	A	0.1007 "	"	14.1 "	0.0474 "	0.0458 "
4	A	0.1248 "	"	17 3 "	0.0581 "	0.0567 "
5	A	0.1003 "	"	13 7 "	0.0460 "	0.0456 "
6	A	0.1200 "	"	16.6 "	0 0556 "	0.0545 "
7	B	0.0517 "	Na_2CO_3	7.1 "	0.0238 "	0.0235 "
8	B	0.1057 "	$LiCO_3$	14.1 "	0.0474 "	0.0480 "
9	B	0.1255 "	"	16.8 "	0.0564 "	0.0570 "
10	C	0.0908 "	Na_2CO_3	12.0 "	0.0403 "	0.0412 "
11	B	0.1098 "	$LiCO_3$	14.6 "	0.0491 "	0.0499 "
12	B	0.1015 "	"	13.4 "	0.0450 "	0.0461 "

In No. 11 and No. 12 precipitation was made in the presence of 25 per cent. NH_4OH, specific gravity 0.90.

The uric acid "A," as previously indicated, was not a recrystallized product, which probably accounts for the slight plus error found in several instances.

DETERMINATION OF URIC ACID DISSOLVED IN A URINE FROM WHICH THE PURIN BODIES HAD BEEN PREVIOUSLY REMOVED. The purin bodies were removed from a urine by adding Salkowski's Ag solution in excess and sufficient NH_4OH to dissolve all AgCl. After filtering the urine was acidified with HNO_3, allowed to stand, and the AgCl filtered off. In order to confirm the fact that the urine now contained neither purin bodies nor silver, a definite quantity of $\frac{N}{50}$ Ag solution was added, and this titrated with the $\frac{N}{50}$ KI under the exact conditions in which the following analyses with definite quantities of uric acid were made, with the result that the correct agreement in the titre was found.

The uric acid "A" was invariably dissolved in 10 to 20 c.c. of a saturated solution of $LiCO_3$ in the cold; 55 c.c. $\frac{N}{50}$ Ag solution were then added, followed by about 90 c.c. of the purin-free urine and 55 c.c. NH_4OH, specific gravity 0.90. The solution was diluted finally to exactly 220 c.c. with the same urine. The solution thus contained 25 per cent. of strong NH_4OH. As usual, two portions

of 100 c.c. each were filtered off and the determinations made with these two solutions.

Number of experiment.	Total uric acid dissolved.	$\frac{N}{50}$ Ag required.	Uric acid found in 100 c.c.	Uric acid added in 100 c.c.
1	0.1095	14.7	0.0494	0.0498
2	0.1006	13.5	0.0456	0.0457
3	0.1030	14.0	0.0471	0.0468
4	0.1290	17.3	0.0581	0.0586
5	0.0824	11.2	0.0376	0.0375
6	0.1021	13.6	0.0457	0.0464
7	0.0595	7.9	0.0265	0.0270

No. 7 was a uric acid from urine.

COMPARISON OF THE NEW METHOD WITH THE LUDWIG–SALKOWSKI METHOD. The Ludwig-Salkowski method has by common consent been accepted as the standard method for determining uric acid in urine. The method, however, is far from being an ideal one aside from the time factor. Leaving out of account entirely minor errors for which corrections can be made, or which with care may partially be avoided, there are, in addition, certain gross errors which can materially affect the results obtained.

Geelmuyden[1] has shown in a series of fourteen determinations that invariably a lower result is obtained by making nitrogen determinations on the uric acid as eventually separated in the course of the method than by weighing the precipitate. The differences in the two procedures amounted to as much as 22.4 per cent. in one case, and the average difference found was 9.3 per cent. It is true that Geelmuyden weighed the uric acid in the objectionable paper filter and did not remove the sulphur from the precipitate, yet these points alone do not account for the marked discrepancy found.

Again, the Ludwig-Salkowski method depends upon a weak HCl solution to finally separate the uric acid from the purin bases.[2] It is, however, a fact[3] that both xanthin and guanin are soluble with difficulty even in strong HCl, consequently in a urine which contains these substances in comparatively large amounts the uric acid thus separated will be contaminated by them and the result vitiated to this extent.

In the following analyses the Ludwig-Salkowski method was followed as described in Huppert's work. One modification was made in regard to the final weighing of the uric acid.

It was our experience that instead of it being the exception that Ag_2S should separate with the uric acid, this was rather the rule; moreover, the amount was quite appreciable. Thus, in two cases in which the amount was determined, we found 7.9 mg. and 11.1 mg. To remove this Ag_2S by means of alkali hydrate, as has been

[1] Zeitsch. f. Analyt. Chem., 1892, 31, 160.

[2] Salkowski's Pract., S. 251.

[3] Huppert in Neubauer und Vogel Analyse des Harns, 1898, pp. 338, 344, 350.

proposed, would introduce as great an error by the decomposition of the uric acid as the one it was intended to correct. For this reason, acting upon the advice of Dr. E. E. Smith, we collected the uric acid in a Gooch crucible, and after drying to constant weight ignited and calculated the uric acid by the loss in weight. Although by this means we do not entirely eliminate the error due to contamination by Ag_2S, since the sulphide is converted into oxide, still the error is reduced to a minimum.

In the following analyses it will be seen that in most cases the agreement between the Ludwig-Salkowski method and the new method is close, but that in some cases considerably more uric acid is found by the Ludwig-Salkowski method. This, we believe, is due to the fact, as pointed out above, that in the Ludwig-Salkowski method the uric acid can easily become contaminated by some of the more insoluble purin bases, should these be present.

In each case 100 c.c. were used in carrying out the Ludwig-Salkowski method. The new method was followed as previously described.

Analysis number.	Uric acid by new method in 100 c.c.	Uric acid by Ludwig-Salkowski method in 100 c.c.	Description of urine used.
1	0.0598 gr.	{0.0609 / 0.0612}	Normal.
2	0.0437 "	0.0436	Normal of pregnancy.
3	0.0504 "	0.0506	Normal of pregnancy.
4	0.0961 "	{0.0964 / 0.0992}	Leukæmic.
5	0.1015 "	{0.1040 / 0.0994}	Leukæmic.
6	0.0745 "	0.0758	Enteric fever.
7	0.1008 "	0.1027	Tubercular pneumothorax.
8	0.0658 "	{0.0744 / 0.0701}	Normal.
9	0.0370 "	0.0413	Leukæmic.
10	0.0631 "	0.0687	Normal.

DETERMINATION OF THE TOTAL PURIN BODIES. *Comparison of the New Method with Arnstein's Modification of Camerer's Method.*[1] In this method the purin bodies are determined by making nitrogen (Kjehldal) determinations on the silver precipitate, care having been taken to remove the last traces of NH_4OH from the precipitate by boiling it with water and magnesia. In the following analyses the total purin bodies were calculated as uric acid.

A comparison of the results obtained based on the uric acid is sufficiently accurate for all practical purposes. Since, however, in the one case we calculate the uric acid from the N content, and in the other case from the Ag content, a strictly accurate comparison is impossible, in view of the fact that we are dealing with a heterogeneous mixture.

[1] Zeitsch. f. Physiol., 1897, Ch. 23, 426; Med. Wissensch., 1898, 15, 257.

Number of analysis.	Total purin bodies by Arnstein's modification of Camerer's method in 100 c.c. urine.	Total purin bodies by new method in 100 c.c. urine.
1	0.0816 gr.	0.0846
2	{0.0777 / 0.0787} "	0.0793
3	0.0814 "	0.0852
4	{0.0651 / 0.0661} "	0.0665

DETERMINATION OF THE TOTAL PURIN BODIES IN URINES TO WHICH KNOWN AMOUNTS OF URIC ACID HAD BEEN ADDED. The total purin bodies were determined in a urine by the new method as previously described, and the result calculated as uric acid.

To 110 c.c. of the same urine a definite quantity of uric acid dissolved in a cold saturated solution of $LiCO_3$ was then added, the purin bodies precipitated by 55 c.c. $\frac{N}{50}$ Ag solution, and the final dilution brought up to 220 c.c. with water. The determinations were then made as before in two portions of 100 c.c. each, and the results calculated as uric acid.

Experiment number.	Purin bodies in 50 c.c. urine.	Uric acid added to this urine.	Total purin bodies found in 100 c.c.	Uric acid actually added to 100 c.c.	Uric acid found.
1	0.0302	0.0922	0.0736	0.0419	0.0424
2	0.0302	0.0823	0.0675	0.0374	0.0374
3	0.0356	0.0752	0.0708	0.0342	0.0352

No. 3 contained uric acid obtained from urine.

In conclusion, we will call attention to the following points: We found that a few drops of chloroform added to urine will prevent decomposition of the purin bodies. In several instances a urine to which chloroform had been added gave the same result after standing seventy-two hours as was obtained originally.

If the urine contains a uric acid deposit this should be brought into solution either by warming, or, what will usually be found necessary, by dissolving this deposit in a small quantity of a saturated solution of $LiCO_3$.

If a urine contains KI this must be removed by adding $AgNO_3$ in excess and then a chloride to remove the excess of Ag.

Albumin and sugar apparently exert no deleterious influence.

The method as proposed deserves the designation of "a clinical method" in the sense that it places at the disposal of the clinician an accurate method for the determination of both the total purin bodies and the uric acid, determinations that can be made in a short period of time—far shorter than by any of the numerous other methods that have been proposed. On the other hand, the term "clinical method" is looked upon by chemists, not without good reason, as a term indicating a method grossly inaccurate, and in this sense the method does not deserve to be known as a clinical method.

THE VASOMOTOR FACTOR IN THE CLINICAL MEASUREMENT OF THE BLOOD PRESSURE.[1]

By Albert Abrams, A.M., M.D.,
of San Francisco, Cal.

In this contribution specific reference will be made to blood pressure observed in arteriosclerosis. To me one of the most paradoxical manifestations of arteriosclerosis is the pronounced high blood pressure coupled with the local evidence of cardiac incompensation. The latter refers specifically to the enfeebled heart revealed by cardiac auscultation. In other words, the cardiac tones are weak, whereas the blood pressure is relatively high. In his studies in stethophonometry[2] the writer was better able to appreciate the foregoing fact than he would be were he guided by the conventional method of cardiac auscultation. The stethophonometer is a little piece of mechanism with coarse and fine adjustment attachable to the stethoscope containing a composition material which offers gradual increasing resistance to sound. The stethophonometer demonstrates that the intensity of the heart tones is no accurate gauge of heart strength. The instrument in question enables one to differentiate the muscular and valvular components of the heart sounds, and serves further to distinguish murmurs of valvular and muscular genesis.

Another important aid furnished by the instrument is in recognizing organic from inorganic cardiac murmurs and autochthonous from transmitted murmurs. Elsewhere[3] the writer has referred to inhibition of the heart as an aid in diagnosis. This manœuvre took into consideration the fact that the intensity of a cardiac murmur was dependent on the vigor of the heart. Loud murmurs often become weak or disappear in the course of febrile affections and in the moribund state owing to the slow and feeble action of the heart. The expedient in question seeks to slow the action of the heart, and in its execution we are constrained to rely on the efforts of the patient. This is not necessary if the stethophonometer is employed. By interposing increasing resistance to transmission inorganic and transmitted murmurs may be made to disappear to be replaced by tones. The stethophonometer has taught the writer that the unreserved reliance placed on the tonometer and other instruments for gauging blood pressure in arteriosclerosis is unwarranted by clinical evidence. It is usually taught that when the

[1] Read by invitation before the Oregon State Medical Association, Portland, Oregon, August 30, 1904.

[2] Abrams. Diseases of the Heart, 1900, p. 169; Medical News, July 8, 1899; New York Medical Journal, October 18, 1902.

[3] Philadelphia Medical Journal, September 29, 1900.

tonometric figure is low, with clinical evidence of arteriosclerosis, it is a sign of failing heart power. The tonometer and other like apparatus are constructed on the general principle that, after the blood supply to a part is inhibited by compression, the gradual removal of the latter will relieve the obstruction, and, when the point is attained at which the intra-arterial is greater than the extra-arterial or capillary pressure, it is indicated by a gauge which registers the blood pressure.

Now, in arteriosclerosis even the smallest bloodvessels (arterio-capillary fibrosis) are firm and unyielding, hence the compression of such vessels for gauging blood pressure conduces to erroneous results. Three factors make up the normal blood pressure, viz., force of the ventricle, frictional resistance of the capillaries, and arterial elasticity.

If the heart is weak, as is manifested by an enfeebled second aortic tone, increased blood pressure can never indicate a vigorous heart action, as is currently supposed. I am, therefore, constrained to conclude that in estimating the vigor of the myocardium blood pressure is of subsidiary value only and then when coupled with cardiac auscultation. There is unquestionably a vasomotor factor concerned in the maintenance of high blood pressure when cardiac enfeeblement coexists. I fully realize that I am running counter to orthodox teaching when I assume the contention that relatively high blood pressure is the necessary corollary of a weak heart. Compensation in cardiac anomalies is not necessarily confined to an increased capacity for work of the heart musculature, for there are many other compensatory factors, as, for instance, the augmentation of vascular tone in mitral stenosis and the diminution of the same tone in aortic regurgitation. We are in a position to estimate the degree of myocardial insufficiency, but the sufficiency of vasomotor and nerve influences in maintaining the circulation has heretofore baffled the efforts of clinical interpretation. Whereas, it is true that augmented peripheral resistance represented by increased function of the vasomotor nerves calls forth the latent energy of the heart, such increase in energy is fully compensated by the diminution in the number of heart beats. In general, increased blood pressure denotes a diminished and lowered blood pressure, an increased frequency of the pulse. One cannot gainsay that of the two conditions, increased blood pressure and increased energy of the heart, the former is preferable.

The blood supply to the heart occurs during diastole, and inasmuch as an increased pulse rate is at the expense of diastole, the nutrition of that organ must necessarily suffer. The nutrition of the heart is dependent on the pressure in the aorta, and when this sinks less blood is propelled into the coronary arteries. Such is the inconsistency of the average practitioner that, while he looks askance at high blood pressure and endeavors to subdue it, he does not

hesitate to goad the heart by cardiotonic medication. Increased peripheral resistance of the bloodvessels serves as a prop to the enfeebled heart. We are inclined to forget that the elastic reaction of the arterial walls is an important factor in aiding the circulation of the blood, in fact, the arterial system is a subsidiary heart.

A rigid artery even in early arteriosclerosis is of no earthly benefit to its possessor; indeed, it is an incumbrance, yet that very artery may be made to yield its modicum of duty by augmented activity of the vasomotor system of nerves which puts it in a condition of moderate contraction. Thus the nervous system may compensate an impaired myocardium. That the bloodvessels are by no means a subordinate factor in furthering the circulation is evidenced by the recent observations of Hasebroek.[1] This writer tentatively proclaims a new theory based on the fact that there is a propulsive energy at the periphery independent of that in the heart, and that the periphery represents another second independent pumping apparatus, coupled with that of the heart. The periphery has not only its elastic contraction and expansion, but also its active diastole and systole in the arteries. This diastolic systolic activity is manifested in the capillaries as a sucking-in, an inspiration, as it were, while in the arteries it is more of a propulsive energy. Both these forces combine to create an independent and forcible stream into the veins which are passive and merely serve as a passive reservoir for the blood stream.

It is generally conceded that all of the factors that make up blood pressure the resistance offered by the bloodvessels is paramount. If the vessels are dilated, the pressure falls; if contracted, it will rise.

The nervous mechanism which presides over the tonus of the bloodvessels is the vasomotor apparatus, and while the latter I concede may be reflexly influenced by irritation from the bloodvessels themselves or from the end organs of sensory nerves in general, we are inclined to forget that the vasomotor apparatus may operate independently of such influences. Emotions and the state of the mind in general greatly influence the calibre of the bloodvessels through the vasomotor system of nerves. Take neurasthenics for a paradigm, and I have examined a large number of them at different periods under emotional influences, intense mental application, and when their brains were at rest, and in each instance my results varied. Emotional influences and intellectual application increased blood pressure, while mental rest reduced it. Again, increased cardiac pressure does not react equally on all the bloodvessels, and this is evidenced by the fact that the blood pressure in both radials is not always the same. Physical activity, the ingestion of food, menstruation, and other conditions also modify blood pressure. Another and more important factor influencing blood

[1] Deutsche Archiv f. klin. Med., Berlin, Bd. lxxvii. Nos. 3 and 4.

pressure is the heart volume, which is continually subject to reflex conditions. The writer has repeatedly demonstrated the occurrence of the *heart reflex* as a result of nasal and gastric irritation as well as by irritation of the skin over the precordial region. The writer's heart reflex has been repeatedly confirmed notably by Merklen and Heitz[1] and Heitler.[2]

The writer has recently demonstrated also a heart reflex of dilatation, aortic reflexes and myopathic and psychic heart reflexes,[3] facts which still further suggest variations in heart volume and changes in blood pressure. Without entering further into a discussion of these preliminary facts we may at once proceed to determine if possible how the clinical vasomotor factor may be excluded in estimating the blood pressure. In the following investigations the Riva-Rocci instrument was employed in gauging blood pressure. After the blood pressure was determined according to the customary method, the patient was instructed to inhale nitrite of amyl from a bottle, after which procedure the blood pressure was again estimated, and the difference noted. The arm-piece of the instrument need not be removed until the investigations are completed.

It is wise to instruct the patient not to practice forced breathing while inhaling the amyl nitrite, as observation has taught me that this physiologic act will reduce blood pressure and thus negative the clinical findings. Sufficient of the drug must be inhaled to induce the physiologic action, viz., slight duskiness of the face, fulness in the head, and relaxation of the bloodvessels. A few words noted elsewhere[4] are here apposite with reference to the physiologic action of the drug.

Amyl nitrite will intensify feeble cardiac murmurs, but ordinarily it is not serviceable in diagnosis, owing to the creation of cardiomuscular murmurs, which have no reality other than in the delirious state of the organ.

To bring out aneurysmal pulsations while the *x*-rays are traversing the chest, it is indispensable, although the aortic reflexes are more available in this regard.

During the inhalation of amyl nitrite in a certain percentage of persons the transverse diameter of the heart will become diminished. This drug is almost a specific in inhibiting the distress of angina pectoris, and if it reduces the cardiac area as the writer has demonstrated, the theory of Heberden, that angina pectoris is a cramp of the heart muscle, must be wrong. The theory of extreme tension of the ventricular walls in consequence of acute dilatation seems to be corroborated by the action of the drug upon the heart.

I have observed another phenomenon associated with the inhala-

[1] La presse médicale, August 1, 1903.
[2] Wiener klin. Wochen., 1890; and Centralbl. f. d. ges. Therapie, 1893.
[3] American Medicine, January 3, 1903.
[4] Ibid., July 16, 1904.

tion of amyl nitrite, and that is a limited patch of dulness which develops over the manubrium sterni.

This patch of dulness may involve the entire manubrium and extend to the right as well as to the left side. The dulness in question is almost never reproduced after an immediate second inhalation of the drug. The dulness is caused by circumscribed collapse of lung (the lung reflex of contraction). In some persons inhalation of the drug evokes dull areas in other chest regions, but the manubrium dulness is practically constant. The latter area of dulness may at once be dissipated by tapping the epigastrium, which provokes the counter lung reflex of dilatation. In the following table the blood pressure of ten average normal individuals is presented showing the influence on blood pressure after inhalation of amyl nitrite during the time that the face of the patient was flushed, the latter being in the sitting posture:

Case.	Age.	Blood pressure before and after inhalation of amyl nitrite.	
		Before.	After.
1	10	115 mm.	125 mm.
2	13	125 "	145 "
3	20	133 "	140 "
4	20	140 "	143 "
5	25	135 "	139 "
6	19	128 "	128 "
7	33	148 "	150 "
8	25	134 "	142 "
9	27	158 "	160 "
10	36	153 "	165 "

In the foregoing table one notes that the average effect of amyl nitrite inhalation in the normal individual is to cause a slight inincrease of blood pressure.

One may also observe in the examination of the normal individual that the primary effect of the inhalation is to slightly depress the blood pressure, but it rises at once. I am inclined to conclude that in the average healthy person the inhalation of amyl nitrite relaxes the arterial wall by elimination of the vasomotor influence, thus bringing into play the veritable cardiac pressure.

An examination of many arteriosclerotics after the foregoing procedure prompts me to classify them as follows:

1. Arteriosclerotics with high blood pressure and strong cardiac tones who show after inhalation of amyl nitrite a stabile or a slight rise of blood pressure, as is demonstrated by the selection of the following subjects:

Case.	Age.	Blood pressure before and after inhalation of amyl nitrite.	
		Before.	After.
1	62	157 mm.	163 mm.
2	68	210 "	210 "
3	58	160 "	165 "
4	60	168 "	168 "
5	64	174 "	176 "

2. Arteriosclerotics with high blood pressure and enfeebled cardiac tones, who show after the inhalation a decided decrease of blood pressure. In these as well as in the succeeding class the reduction in blood tension was no doubt influenced by the elimination of the tonus of the arteries, which was maintained by the vasomotor system of nerves, thus allowing the true endocardial pressure, which was enfeebled, to be brought into action.

Case.	Age.	Blood pressure before and after inhalation of amyl nitrite.	
		Before.	After.
1	74	218 mm.	190 mm.
2	59	240 "	195 "
3	62	200 "	175 "
4	71	210 "	180 "
5	60	290 "	240 "

3. A final class of patients with arteriosclerosis with relatively low blood pressure and enfeebled heart tones who demonstrate a still further reduction of blood pressure after inhalation of amyl nitrite, as the following table shows:

Case.	Age.	Blood pressure before and after inhalation of amyl nitrite.	
		Before.	After.
1	53	125 mm.	115 mm.
2	60	120 "	115 "
3	65	150 "	125 "
4	70	130 "	120 "
5	61	135 "	130 "

In a prognostic sense the patients in the last class belong to the hopeless category, insomuch as the vasomotor system of nerves is either exhausted or unable to properly usurp the functions of a failing heart.

Desirous of determining the influence of digitalis on some of the preceding cases, I have selected from the second class of arteriosclerotics Cases I. and V. and from the third class Cases II., IV., and V. A tablespoonful of a reliable infusion of digitalis was administered three times a day for five days, when it was presumed that the digitalis had brought about its physiological effects, and the following results were attained:

Class.	Case.	Blood pressure after using	
		Digitalis.	Amyl nitrite.
2	1	215 mm.	150 mm.
2	5	240 "	200 "
3	2	160 "	130 "
3	4	140 "	130 "
3	5	140 "	135 "

Digitalis is the sovereign heart tonic, and is correctly specified as the quinine of the heart. All heart tonics are divided into direct and indirect: the former acting by direct stimulation of the heart, the latter by improving the nutrition of the organ or by relieving vessel tension hastening the output of blood from the heart.

The digitalis substances in the therapeutic stadium have a dual action by slowing the pulse and augmenting the blood pressure. The latter is the product of two forces, viz., increased heart work and augmentation of the vessel tone.

The action on the heart of the digitalis substances is to increase the work of both ventricles, but in not a few instances increased work on the part of the left ventricle signifies an increased blood pressure which is very often an undesirable condition, as in nephritides and arteriosclerosis. It is usually taught that high blood pressure as in arteriosclerosis is a contraindication for the administration of digitalis, although Sahli[1] has demonstrated that in conditions of stasis with increased peripheral resistance digitalis possesses a paradoxical action, insomuch as it combats the stasis and reduces the blood pressure. Some of the theories established for the purpose of creating indications and contraindications for the administration of digitalis suggest the comment of the mathematician, who, having demonstrated a new mathematical theory, thanked God that it could not be of the slightest utility to any living soul. Many of the theories in question also remind me of the erudite German professor of economics who received a bed as a present. Until the small hours of the morning he busied himself with abstruse calculations to determine whether he was large enough for the bed or if the latter were large enough for him. Finally, he was struck with the happy idea of getting into the bed, and to his intense delight discovered that it was admirably suited to his proportions.

So it is with digitalis; this valuable cardiotonic is often relegated to oblivion owing to the numerous theories which indicate and contraindicate its employment.

No theory can guide the practitioner in the use of digitalis, and its tentative administration is always warranted, provided the physician begins with small doses and is prepared to recognize its untoward effects.

I have never permitted the high blood pressure nor the tortuous arteries in arteriosclerosis to thwart me in the use of digitalis, and my temerity, if it may be so specified, has rarely guided me into error. Very true, my conception of blood pressure in arteriosclerosis may be heterodoxical, and it is perhaps for this very reason that I have ignored the circumspection of the doctrinaire.

The cases cited in the table showing the effects on blood pressure after the use of digitalis may serve as a vehicle for my contention. In Class 2, Case I., the blood pressure before using digitalis was 218 mm., and after inhalation of amyl nitrite it was reduced to 190 mm. After the use of digitalis it was 215, but the inhalation of amyl nitrite reduced it to 150 mm. Now, the theory of action of the drug on the patient is practically as follows: The blood pressure was essentially the same after as before the use of digitalis, but while

[1] Verhandl. d. XIX. Kongr. f. innere Med.

amyl nitrite before the use of digitalis reduced the blood pressure only 28 mm., after its use the pressure was reduced 65 mm. This indicated that the digitalis was unfavorable in its action, for, after the tonus of the bloodvessels was removed by amyl nitrite the greater reduction in blood pressure demonstrrated the cardiac force was further reduced after than before the use of digitalis. In other words, digitalis was goading a jaded heart, and the high blood pressure was illusory. This action is not uncommon in the administration of digitalis, owing to its vasoconstrictor influence, and when the latter action implicates the coronary bloodvessels the nutrition of the heart must suffer. In such instances, in determining the action of digitalis, we must often decide whether prolongation of the diastole can compensate for the defective nutrition.

In the case last cited the action of digitalis was unfavorable, but when it was given in combinatiom with *diuretin*, which seems to antagonize the vasoconstrictor components of digitalis, the action of the latter drug was more favorable, the blood pressure falling only 15 mm. in lieu of 65 mm.

This combination of diuretin with digitalis in arteriosclerosis is more often advantageous than the combination of the latter drug with nitroglycerin. Very frequently the use of a brisk purgative in arteriosclerosis—*e. g.*, a combination of calomel and jalap for the purpose of unloading the bloodvessels—will be productive of more good than anything else, and will also further the action of digitalis and other cardiotonics. Whereas, the degree of passive hyperæmia of the lungs may be regarded as a gauge of the functional capacity of the right heart ventricle so, also, may the size of the liver be utilized as a guide of venous stasis, for the latter organ is practically a reservoir for the right ventricle. Even in the early stages of cardiac insufficiency the liver enlarges, whereas in the later stages the systolic liver pulse indicates that a tricuspid insufficiency has been added to dilatation of the right ventricle.

What I have called the cardiosplanchnic phenomenon serves a useful purpose in determining the grade of congestion in the splanchnic area. This phenomenon is based on the experimental investigations of Hill and Barnard,[1] who demonstrated that there is a tendency for the blood to accumulate in the splanchnic area, and that the great splanchnic veins are very susceptible to pressure, and that a large quantity of blood may be squeezed out of them by firm compressions of the belly with the hand. If a series of firm abdominal compressions with the hand are made in the average individual and the lower sternal region—*i. e.*, the part of the sternum contiguous to the heart is percussed—a pronounced dulness or even flatness will have been found to supersede the normal resonance.

The dulness in question is at once dissipated by a series of deep breaths. This is the cardiosplanchnic phenomenon, and is depend-

[1] Abrams. Splanchnic Neurasthenia, 1904, p. 171, and THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, January, 1904.

ent on the fact that by abdominal compression blood is expressed from the splanchnic veins to the right heart. In some individuals the phenomenon is but feebly expressed, and its degree of expression is proportional to the grade of congestion of the splanchnic veins. If in arteriosclerosis, splanchnic congestion is pronounced digitalin or strophanthin alone or in combination are especially indicated. They are endowed with the property of constricting the splanchnic vessels alone, whereas digitoxin exerts its vasoconstrictor influence on all the bloodvessels. In the action of digitalin and strophanthin we possess a cogent means of relieving the burden of the heart by increasing the receptivity of the peripheral bloodvessels for the blood which has been expressed from the abdominal organs, and the same agents are almost specific in action in relieving splanchnic congestion, which is the underlying condition in splanchnic neurasthenia. For relieving splanchnic congestion the abdominal application of the sinusoidal current is paramount. A few words may be permitted with reference to the action of amyl nitrite. With this drug there is frequently an idiosyncrasy expressed; the subjects are either abnormally susceptible or refractory to its physiological action. In two instances following its inhalation the writer noted a veritable inhibition of the heart and absence of the pulse. The writer recalls a previous statement, viz., that the inhalation of amyl nitrite causes a reduction in the heart volume which is tantamount to a heart reflex, and in the two subjects just cited during the time the drug was inhaled with the *x*-rays traversing the chest the reduction in the heart volume was very much exaggerated above the normal.

A pertinent example of autosuggestion is afforded in one instance from the inhalation of amyl nitrite.

The subject, who had taken chloroform for an operation a few months before, contended while inhaling amyl nitrite that I was giving him chloroform, and in a minute or two he passed into a condition of narcosis, during which time he proved insusceptible to the infliction of pain.

This example of autosuggestion is somewhat analogous to that occurring in the practice of a well-known chloroformist who had occasion to give ether to an hysterical girl who was about to have two small scalp tumors removed.

He found that the ether bottle was empty, and while waiting for a new supply to be brought he instructed the patient how to take deep breaths. After a few deep inspirations she cried, "I am going off," and became unconscious. Both tumors were painlessly removed in this state. It was subsequently learned that the girl had taken ether once before, and the association of ideas merely recalled the effects of ether.

The writer formulates the following conclusions:

1. That blood pressure is an expression of action of two chief factors: ventricular force and vasoconstriction.

2. The inhalation of amyl nitrite will dissipate the vasoconstrictor factor and bring into play the ventricular force, which is the real factor to be encouraged in a failing heart.

3. The vasoconstrictor factor may and does compensate ventricular inadequacy, for it is essential in most cardioarterial diseases for the blood pressure to be maintained to afford better nutrition for the heart and to promote arterial elasticity as a means of establishing the circulation of the blood.

4. The recognition of the ventricular and vasomotor factors in blood pressure serves as a clue in the correct administration of cardiotonics.

5. In the individual endowed with cardiac health the removal of the vasomotor factor causes an increase in blood pressure, whereas the converse condition causes the latter to fall, and the degree of reduction is proportional to the degree of cardiac enfeeblement.

6. The execution of the foregoing manœuvres in estimating heart vigor is by no means comparable to a correct method of cardiac auscultation, although the latter method does not indicate how much of the cardiac force may be attributed to increased peripheral resistance. Cardiac auscultation in conjunction with the sphygmomanometer and the inhalation of amyl nitrite constitute the ideal methods for eliciting the real condition of things.

7. In estimating blood pressure the sphygmomanometer only gauges the force of the left ventricle, and to determine the sufficiency of the right ventricle auscultation of the pulmonic sounds and a physical examination of the lungs are alone adequate.

8. There are certain individuals in whom one finds high blood pressure without cardiac weakness, and after inhalation of amyl nitrite the blood pressure remains the same. Such cases are associated with traces of albumin in the urine, which is of low specific gravity, and are practically instances of incipient chronic interstitial nephritis.

9. It is evident that persistent high blood pressure dependent on augmented tonus of the vasomotor centre is a cogent etiological factor in arteriosclerosis independent of any other cause, and is merely the reaction of arterial overwork.

10. Just as myocardial sufficiency is tested by counting the pulse, first in the erect and then in the recumbent posture, and noting that the less pronounced pulse retardation is in recumbency, the greater the degree of heart insufficiency, so may vasomotor sufficiency be determined. Normally, there is a postural variation in blood pressure. In the erect posture blood pressure rises owing to compensatory arteriole contraction, and this difference between recumbency and standing varies between 15 and 30 mm., according to my measurements with the Riva-Rocci instrument. In vasomotor insufficiency the postural variations are reversed, and this is especially true in neurasthenia, notably the angiopathic form. The bromides, carried to their physiological effects, will cause high blood pressure to fall, if dependent on augmented tonus of the vasomotor centre.

REVIEWS.

OBSTETRIC AND GYNECOLOGIC NURSING. By E. P. DAVIS, A.M., M.D. Philadelphia: W. B. Saunders & Co., 1904.

THERE can be doubt that less instruction is offered upon obstetrics to nurses in the course of their training than upon any other phase of their work. At least this is certainly true in this city, where several of the largest hospitals, those in which the best of training may be procured in general medical and surgical nursing, offer no practical instruction in this department of medicine. This being the case, there is room for a book upon this subject, particularly such a thoroughly good one as this.

The author's long experience in hospital work has placed him in a position to realize the needs of the nurse, and in his book he has carefully refrained from details of treatment and pathology useful alone to the physician, and has very clearly stated the duties of the nurse without, on the other hand, omitting anything of importance for her standpoint. His instructions, moreover, are most comprehensive and definite. For instance, in considering eclampsia he omits its etiology and pathology, contenting himself with detailing concisely the duties of the nurse while awaiting the arrival of medical help, and the same holds true in his discussion of post-partum hemorrhage. The chapter on "Obstetric Surgery" is excellent, and is illustrated in a manner which greatly enhances its value. The chapters upon the care of the newborn infant and the disorders which manifest themselves at this period of life are most satisfactory.

The last chapter in the obstetrical section is devoted to the development of the child, and in its ten pages it covers the ground well.

While most hospitals offer facilities for training pupil nurses in gynecological work there have been but few books published upon the subject for the use of nurses, and our experience has taught us that some such text-book as the present is urgently needed. The author explains the methods of the examination of gynecological cases, and gives among others most satisfactory chapters upon the use of douches, the preparation of the operating-room in private houses, the preparation and after-treatment of operative cases, and concludes with a most valuable appendix upon the preparation of surgical supplies.

We think that a most valuable and indeed the only addition to this portion of the work would be photographic reproductions of the various commonly used gynecological instruments.

W. R. N.

THE PRACTICAL MEDICINE SERIES OF YEAR BOOKS. OBSTETRICS. Edited by JOSEPH B. DE LEE, M.D. Chicago: The Year Book Publishers, 1904.

COMPOSED of a collection of edited abstracts of the best of the articles appearing within the current year, as are all the volumes of this series, there can be no question as to the important use subserved by them. A careful reading of the present volume, for example, will place one in possession of an epitome of the obstetrical advance of the past year which in itself would be ample justification for its publication. Moreover, as all references are, of course, given in full the volume serves as a very valuable index to current literature. Not the least valuable of the matter included is the section devoted to the subject of "Incubation," contributed by the author.

W. R. N.

PEDIATRICS. A Manual for Students and Practitioners. By HENRY ENOS TULEY, A.B., M.D., Professor of Obstetrics in the Medical Department of Kentucky University; Editor of Louisville Monthly Journal of Medicine and Surgery, etc. Illustrated by 33 engravings. Philadelphia and New York: Lea Brothers & Co., 1904.

THIS little volume of 258 pages is one of a series (the Medical Epitome Series) of condensed manuals of pocket-size which is now being published from time to time under the editorship of Dr. V. C. Pedersen, of New York.

The method of arrangement in a continuous text, following the classic text-book model, is a decided improvement over the usual question-and-answer form that has been so extensively used in brief treatises of this character, and thus dogmatic brevity and sacrifice of valuable space are advantageously avoided. The gain in dignity thus secured seems to be discounted to some degree in the volume before us by appending a series of questions at the end of each chapter, convenient as these may be for quizzing purposes. It is to be presumed, therefore, that popular demand has been consulted in retaining this essential feature of the quiz-compend. The subject has been very thoroughly covered from the birth of the infant to adolescence, including essentials of anatomy

and development, the care and hygiene of infancy and childhood, the examination of childish patients, the therapeutic peculiarities of young subjects, and the feeding of infants and older children. Following this the diseases of infancy and childhood are systematically discussed, with the necessary details of nursing and treatment. The style is brisk and pithy, well suited to the limitations of space demanded by the epitomic character of the work. The chapter on Infant Feeding, which is so important a feature of every work on the subject nowadays, is particularly full, covering thirty-three pages, or an eighth part of the whole; and the subject of home modification is discussed very completely. Altogether Dr. Tuley's work seems destined to take rank among the best, if indeed it is not the best, of those of similar scope now before the profession.

T. S. W.

A Manual of Clinical Diagnosis by Means of Microscopic and Chemical Methods for Students, Hospital Physicians, and Practitioners. By Charles E. Simon, M.D. Fifth edition, thoroughly revised and enlarged, illustrated with 150 engravings and 22 plates in colors. Philadelphia and New York: Lea Brothers & Co., 1904.

A book so well known as this one scarcely needs an introduction or detailed review. While the descriptions are concise and accurate, the scope of the book is very comprehensive, including chapters devoted to directions for the examinations of blood, secretions of the mouth, gastric contents, feces, urine, sputum, etc. The present edition has been much enlarged and thoroughly revised. Particularly noteworthy is the chapter upon the blood. Here we find accounts of the latest modifications and newer varieties of hæmatological instruments, as well as valuable and full descriptions of the new methods which have recently come into use for the staining of blood films. Advantage has been taken of the latest researches upon the histogenesis of the leukocytes in devising a classification of these cells. Although there is no encroachment upon the province of the larger text-books of hæmatology, some insight is given into conditions of the blood in various pathological states. The colored plates seem particularly successful. New material has been added to the discussions upon the bacteriology and parasitology of the blood, and, in fact, throughout the book one finds evidences of revision and enlargement. In the section dealing with transudates and exudates the subject of cytodiagnosis receives due attention. In all, the book forms an excellent guide for either practitioner or student, and will be of great practical assistance in the study of clinical diagnosis.

W. T. L.

PROGRESS

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The Chemistry of the Urine in Diseases of the Pancreas.—CAMMIDGE (*Lancet*, March 19, 1904, p. 782) during the last three years has been studying the urine of patients with pancreatic disease in order to determine whether it be possible to recognize lesions of the gland during life as well as to differentiate the character of the lesion. In this investigation he was associated with Mr. Mayo Robson, whose extensive experience in surgery of the pancreatic gland is well known.

As a result of his study, Cammidge claims that it is possible to definitely determine the presence of pancreatic disease from the urinary examination. This is dependent upon the presence of glycerin in the urine, and the urinary test is practically that for glycerose. He asserts that fat necrosis is almost invariably associated with obvious disease of the pancreas. Although it is most typically met with in acute and gangrenous pancreatitis, he believes that it is not improbable that similar but evident changes accompany all forms of pancreatic inflammation. The local fat necroses are dependent upon the fermentative action of the pancreatic secretion. The fat of the tissues is converted into the fatty acids which enter into combination with lime, the other constituent of the fat molecule, glycerin, being absorbed into the circulation. This glycerin is eventually eliminated in the urine, and becomes converted into glycerose when the urine is boiled with a mineral acid, such as hydrochloric acid.

Cammidge describes in detail two tests for glycerose which he terms reaction "A" and reaction "B." Both are modifications of the phenylhydrazine test for glucose. Reaction "A" is briefly as follows: Ten c.c. of filtered urine are poured into a flask; add 1 c.c. of hydrochloric acid; place a funnel in the neck of the flask to act as a condenser and boil gently on a sand-bath for ten minutes. Add 5 c.c. each of filtered urine and distilled water, and allow the whole to cool in running water. Neutralize the excess of acid by adding slowly 4 gm. of lead carbonate, and, after allowing to stand for a few minutes, filter through a moist

filter paper, and wash out the flask on to the filter with 5 c.c. of distilled water. To the clear filtrate add 2 gm. of powdered sodium acetate and 0.75 gm. of phenylhydrazine hydrochlorate, and boil for three or four minutes on the sand-bath. Allow the contents of the flask to cool for twenty-four hours after pouring into a test-tube, and if pancreatic disease be present an abundant flocculent, yellow deposit collects at the bottom of the test-tube, which, when examined microscopically, is found to consist of sheaves and rosettes of yellow crystals. Before carrying out the test sugar must be examined for, and, if present, must be carefully removed by fermentation.

This reaction was not found entirely reliable, because the urine of patients suffering from certain diseases accompanied by active tissue changes, such as cancer, adenitis, pneumonia, etc., sometimes gave a positive result. Eventually reaction "B" was found to differentiate the pancreatic cases. This differentiating test depends upon the fact that the formation of the crystals described in reaction "A" is interfered with in inflammation of the pancreas by a preliminary treatment of the urine with perchloride of mercury, while such treatment does not affect the appearance of the crystals in cases of cancer of the pancreas and the other conditions which give rise to a positive reaction. By a combination of these two reactions Cammidge believes that it is possible to make a trustworthy diagnosis of pancreatic disease in most cases from the urine alone.

In reaction "B," 20 c.c. of filtered urine are thoroughly mixed with half its bulk of a saturated solution of perchloride of mercury. Allow to stand for a few minutes, filter, and to 10 c.c. of the filtrate 1 c.c. of strong hydrochloric acid is added. Boil for ten minutes on a sand-bath, and subsequently dilute with 5 c.c. of the filtrate from the mixed urine and perchloride of mercury and 10 c.c. of distilled water. Allow to cool, neutralize with 4 gm. of lead carbonate, and proceed from this point as in reaction "A."

The next step was to devise some means of differentiating the various forms of pancreatic disease, particularly chronic inflammation and cancer. It was at first thought that the mere size of the crystals would aid in differentiating the various pancreatic lesions. The crystals in malignant disease were, as a rule, coarser and broader than those in simple inflammation. Further, in simple inflammation the crystals from acute cases were, on the whole, somewhat finer than those seen in most instances of chronic inflammation. It was subsequently found that the solubility of the crystals proved more reliable than their size. If the crystals in reaction "A" be observed under the microscope while a 1: 3 dilution of strong sulphuric acid is being irrigated under the cover-slip they will be seen to turn brown when the acid reaches them, and then to dissolve. Experience showed that the solubility of the crystals varied according to the length of duration and nature of the pancreatic disease.

Cammidge summarizes the practical results of urinary examinations in pancreatic disease by these methods as follows: 1. If no crystals are found by either the "A" or the "B" method the pancreas is not at fault, and some other explanation of the symptoms must be sought. 2. If crystals are obtained by the "A" method but not by the "B" reaction active inflammation of the pancreas is present, and surgical interference is indicated. (*a*) The crystals obtained by the "A"

method will in acute inflammation dissolve in 33 per cent. sulphuric acid in about half a minute. (*b*) In chronic inflammation the crystals by the "A" method will take one or two minutes to disappear. 3. If crystals are found in preparations made by both the "A" and the "B" methods there may be (*a*) malignant disease of the pancreas, when the crystals will, as a rule, take from three to five minutes to dissolve, and operation is inadvisable; (*b*) a damaged pancreas due to past pancreatitis, when the crystals will dissolve in from one to two minutes; (*c*) some disease not connected with the pancreas, when the crystals will dissolve in about one minute. In the two latter, (*b*) and (*c*), the urgency of the symptoms and the condition of the patient must decide the need for an exploratory incision.

The writer believes that these methods are also going to be of service in differentiating pancreatic from non-pancreatic diabetes. This belief is based on practical experience with the test in one case of diabetes, which was subsequently shown at autopsy to be pancreatic in origin.

SURGERY.

UNDER THE CHARGE OF

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Osteoplastic Resection of the Symphysis.—MANZ (*Centralblatt für Chir.*, 1904, No. 15) states that the technique briefly consists in a skin incision which should be prolonged from either tubercle of the pubes downward. This incision should be continued downward until the angle of the pubic arch is reached, and all the parts should be freely dissected loose. Then by means of a wire saw the bone should be severed, the direction of the saw being in the direction of the obturator foramen; then taking a periosteal elevator the periosteum should be freely separated, the subsequent cutting of the bone being subperiosteal. By this means the contents of the lower pelvis are most accessible, and extirpation of the prostate or the urethra or the genital organs in women may be done with the greatest ease. When the operation is completed four wire sutures are amply sufficient to approximate the symphysis; then the incision of the skin should be closed in the usual manner.

A New Experiment in the Operative Treatment of Chronic Bright's Disease.—BAKES (*Centralblatt für Chir.*, 1904, No. 14) states that he has had such good results in one case treated by Edebohls' method that it demands to be published: The patient, a man, aged twenty-five years, had been under treatment for ten years in various hospitals

for a chronic nephritis of obscure etiology. Upon his admission to the hospital it was found that his case was typical of this disease, with marked œdema of the legs, ascites, etc. An examination of the urine showed it to be markedly albuminous and full of casts. Operation being decided upon, a bilateral decortication was performed, and the patient made an uninterrupted recovery, eight months later being sufficiently well to return to his usual occupation.

From the experience of this case it would seem that the weak point in Edebohls' method consists in a return of the denuded kidney back into its flat capsule, which of necessity contains but little tissue, and for that reason Bakes in completing the operation merely returned the kidney after removal of as much of this capsule as was possible, and he advises that instead of returning the kidney inside of its capsule, the kidney should either be enclosed in the mesentery or should be dislocated so that it is intraperitoneal when the raw surfaces are brought into intimate contact with the peritoneum. In regard to these two methods of disposing of the kidney, it would seem that it must depend not only upon the size of the kidney, but also upon the condition of the mesentery; and in those cases where the mesentery is found to be atrophied the intraperitoneal method would seem to be the best. In a subsequent operation a decorticized large white kidney was returned and placed between the mesentery, and the patient made an uninterrupted recovery.

Free Serous Exudation of the Peritoneum as an Early Symptom of Perforated Peritonitis.—HAEGLER (*Centralblatt für Chir.*, 1904, No. 10) states that as the result of animal experimentation he has learned that the quantity of the exudate stands in direct proportion to the amount or virulence of the germ material or its toxin that has been introduced. Under the author's direction, Thommen made a series of experiments on animals. Ten c.cm. of normal salt solution was injected intraperitoneally and the animals killed after various periods of time. These experiments showed that within the first six hours the amount of the intraperitoneal fluid was four times greater than the amount that had been injected; it consisted of an opalescent fluid very rich in albumin and which on standing became gelatinous. Intraperitoneal injection into a rabbit of 100 grams of distilled sterile water was followed in a few hours by an increase of from 30 to 40 c.cm. of this same albuminous fluid. The peritoneum reacts to all irritation very rapidly, and this reaction is shown by the excretion of a serous exudate, and it may be stated that absorption occurs in an almost similar length of time. This exudation into the peritoneal cavity is a movement of defence, as it were, on the part of the peritoneum to irritation or infection. In those cases of local inflammation of the intestinal wall the presence of free fluid in the peritoneal cavity should be considered as being unfavorable in weighing up the prognosis of the case. It shows that there is no tendency toward a restriction of the area of inflammation, for as soon as an attempt is made to restrict this inflammation adhesions very rapidly develop.

The Treatment of Supracondyloid Fractures of the Humerus by the Use of the Bardenheuer Extension Apparatus.—GRÄSSNER (*Centralblatt für Chirurgie*, 1903, No. 44) states that the treatment of all

fractures by primary bone suture has for some time been the subject of discussion, but in Germany, at least, this method of treatment for fractures of the shaft of the humerus has been abandoned, and its use reserved for those fractures which are in the region of the ankle-joint. In supracondyloid fractures of the humerus, the Bardenheuer apparatus suitable for a fractured tibia is the one usually employed; however, in exceptional cases, where the fragments are widely separated it is best to use extension by weights, the forearm being placed in supination. The author notes five cases in which this method of treatment was most successful, while in another case the result was not so good. Passive motion of the elbow should be begun on the twelfth day, and this should be followed by careful massage of all the arm after the removal of the apparatus.

The Treatment of Gallstones Found as a Coincidence in Abdominal or Pelvic Operations.—CLARK (*American Medicine*, 1904, No. 2), after an admirable review of this most important subject, states, in conclusion: 1. The usual statement that 95 per cent. of gallstones produce no symptoms is fallacious, because it is drawn from autopsy and dissecting-room statistics. 2. Recent research points very strongly to the bacteriological origin of gallstones. 3. Bile is not bactericidal, for in the majority of cases of cholelithiasis micro-organisms of a more or less pathogenic nature are discovered. 4. Under these circumstances many more or less vague symptoms attributed to gastrointestinal or general constitutional disturbances may arise from toxins elaborated around these foreign bodies in the gall-bladder. 5. All clinicians admit that there is a wide hiatus in the clinical symptoms between the early formation of gallstones and the so-called classic attacks of biliary colic with jaundice. 6. Abdominal surgeons should make a most careful record of all gastrointestinal or hepatic symptoms and other vague epigastric pains, and associate these with an examination of the gall-bladder, with a view to establishing a further link in the symptomatology of cholelithiasis. 7. As cholelithotomy in a large series of cases has been attended with less than 2 per cent. mortality, the coincident removal of gallstones with some other abdominal operation is not a hazardous undertaking. 8. In the author's series of cases more than 50 per cent. have shown symptoms which could be unquestionably or with great assurance attributed to the presence of gallstones. 9. This coincident operation should be dictated by the most careful surgical judgment, for if the patient is in a critical condition from a prolonged operation, or the primary operation has been a septic one, this extra operation may be attended by serious results.

On the Prophylactic Use of Morphine in Cases of Severe Cerebral Injury.—MACDOUGAL (*Lancet*, June 25, 1904) states that his attention was attracted to this subject by the paper by Barr in the *British Medical Journal*, November 18, 1899, on "Meningitis," in which he calls attention to the excellent results that followed its employment in cases of this disease, and clearly showed that its beneficial action was due to the physiological effect upon the vascular and nervous systems inducing that condition of rest which, as Mr. Hilton has so admirably taught, is nature's opportunity. The author reports in detail three cases of very severe cerebral injury in which the sulphate of morphine in doses

of one-sixth of a grain hypodermically were administered from time to time, and the patients all made uninterrupted recoveries. All of the patients were subjected to operative interference as soon as they were seen. In all of the cases the use of the drug was continued for at least a fortnight at intervals of from six to eight hours, and its use would seem indicated in all cases of severe cerebral traumatism.

THERAPEUTICS.

UNDER THE CHARGE OF

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Electricity in Facial Neuralgia.—DR. G. DIMIER believes that the use of the continuous current is followed by the best of results in this condition. Certain observers advocate the use of a weak current—two to ten milliampères—while others prefer a current of from twenty to eighty milliampères; the author, however, considers the weaker current to be of sufficient strength. The negative electrode is placed at the back of the head, while the positive, which is of sufficient size to cover the distribution of the affected nerve, is placed upon the cheek. At each séance the current is applied from forty minutes to an hour. After the removal of the electrode the skin is red and congested, but this manifestation disappears within a few hours, leaving no trace, although desquamation may follow. After the séance the patient will experience relief and often a desire to sleep. Two or three treatments per week are sufficient in light cases, while daily applications are necessary in those of severity; it is also necessary that the treatments be at the same time of day, regularity and periodicity being essential. One should not be discouraged if no betterment is evident at the beginning, but the patient must be encouraged to persevere. At least three months are necessary to achieve a cure, the best method being daily or tri-weekly applications for this period, and eight or ten applications per month for several following months.—*La Quinzaine Therapeutique*, 1904, No. 7, p. 164.

The Treatment of Cutaneous Infections in Infants.—DR. D'ASTROS discusses the local and constitutional treatment of these conditions as follows: The first indication is to sterilize the lesions so as to prevent further infection. This is best accomplished by means of a bath of 1:15,000 mercury bichloride, or an application of soap and water followed by naphtholated vaseline (1:10). Irritating applications are to be guarded against, lest they lessen the resisting power of the healthy skin and lead to a spread of the infection. Consequently the daily bath should be of simple boiled water, with the addition at times of a little sodium bicarbonate or boric acid. The dressings to be preferred are of simple sterile gauze. Zinc ointment combined with small quantities of boric or salicylic acid makes the best moist application,

while the most useful powder is a mixture of zinc oxide, talc, and bismuth subnitrate. Certain therapeutic applications, such as solutions of zinc or copper sulphate, are useful in impetigo, while in purulent conditions hydrogen peroxide is an acceptable antiseptic. Iodoform is powerful in this connection, but has disadvantages. Its use should be reserved for certain forms of ecthyma and cutaneous gangrene. In furunculosis, after proper washing with antiseptics and smearing of the surrounding parts with 10 per cent. boric acid in vaseline, the lesions should be incised, drained, and dressed with dry gauze. General treatment consists in proper feeding and hygiene, fresh country or sea air, tonics, and, in marked cachexia, subcutaneous injections of normal salt solution.—*Journal de Médecine de Paris*, 1904, No. 23, p. 232.

Euquinine in Malaria.—Large doses of this drug, according to DR. K. B. BUDBERG, produce none of the unpleasant effects of quinine, and it is at least as powerful against malaria as the latter agent. On account of its lack of bitter taste it is easily administered to children, and its solubility in alcohol is an additional recommendation. It is an important fact that euquinine in sufficiently large doses (not less than 15 grains), and given about six hours before, will prevent an expected paroxysm. Smaller doses may have a like effect or only lessen the intensity of the paroxysm, or cause it to appear at irregular intervals. A single dose of from 15 to 20 grains often will, in recent cases, prevent further chills, but in chronic cases a recurrence is likely to take place within a week or two.—*St. Petersburger medicinische Wochenschrift*, 1904, No. 6, p. 53.

The Treatment of Itching.—M. F. TRÉMOLIERÈS considers the ideal treatment to be that which strikes at causes and regulates the polyuria, the oliguria, the hypoazaturia, the albuminuria, the cholæmia, the intestinal insufficiency, or whatever produces the pruritis. Various drugs taken internally may influence this distressing symptom—the author considers carbolic acid, gelsemium (which he believes dangerous), valerian, atropine sulphate, or valerianate (by mouth), arsenious acid, hydrocyanic acid, asafœtida, etc. In the pruritus of digestive origin and in senile and vulvar pruritus he recommends lactic acid, 6 to 10 drops of a 1 per cent. solution for infants; 15 to 30 drops for adults. External applications may be in the form of lotions, powders, or pomades. The following comprehensive formula is suggested: hydrocyanic acid, ½ to 1 part; mercury bichloride, ½ to 1 part; copper sulphate, 1 to 5 parts; carbolic acid, 5 to 10 parts; resorcin, 5 to 20 parts; chloral, 5 to 25 parts; potassium bromide, 5 to 50 parts; water, 1000 parts. Lotions of menthol and ichthyol, powders of bismuth, zinc oxide, salol, and salicylic acid are mentioned, as well as ointments of potassium cyanide, morphine, cocaine, belladonna, and calomel. Pruritus of the anal and genital regions may be treated by suppositories, lotions, and douches of very hot water, either pure or medicated. Above all, the local lesions, such as fissures, parasites, irritating discharges, etc., should be corrected. Moist dressings of 5 to 10 per cent. silver nitrate solution are useful here. Various physical means, the chief of which are hydrotherapy, electrotherapy, cutaneous occlusion, and climatotherapy are proper adjuvants in treatment.—*La presse médicale*, 1904, No. 51, p. 401.

PEDIATRICS.

UNDER THE CHARGE OF

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Status Lymphaticus, with Report of Cases.—R. A. BIECHELE (*Archives of Pediatrics*, July, 1904) carefully reviews the morbid anatomy of status lymphaticus, and reports several interesting cases.

The first case, although unconfirmed by post-mortem examination, is by reason of its history and course classed as status lymphaticus. The child, eleven months old, had been observed for the first time when six months of age. At that time she had enterocolitis, with thymic asthma and several slight convulsive seizures. Percussion revealed a marked increase of dulness in the region of the thymus; the tonsils were large, adenoids prominent, and there was some enlargement of the superficial lymph nodes. She recovered from the enterocolitis and remained well until the final attack. Following a slight fall convulsions supervened and continued for several hours. Then thymic asthma developed, which was followed by a short period of coma, and again convulsions, which continued until death occurred, twenty-four hours after the receipt of an injury so slight that under ordinary circumstances it would have passed unnoticed.

The relation of status lymphaticus to infection is illustrated by the following case: This child, twenty-two months of age, had always been in good health until the present illness. There had been a house epidemic of influenza, and this patient contracted the disease, which was typical, but apparently of mild character. Upon the second day, without premonitory symptoms, he developed convulsions, epileptiform in character, occurring at first at intervals of about thirty minutes. But in about two hours the convulsive explosions recurred with such rapidity as to be almost constant, and continued until death, about four hours after the first seizures and twenty-five hours from the time of the first evidence of infection.

The autopsy showed body well developed and nourished, with rickety manifestations. Upon opening the thorax a very large thymus presented itself, reaching from above the episternal notch well down over the pericardium and having two large lateral lobes. The organ weighed fifty-two grams, but the trachea was not compressed to any great degree. The heart and lungs were normal. The bronchial lymph nodes were enlarged. The spleen was enlarged, but of normal consistence. The agminated glands of the ileum were very large and elevated. The solitary follicles throughout the large intestine were very conspicuous. The mesenteric lymph nodes were exceedingly numerous, and upon section were succulent and of a translucent gray color. The

stomach was all but completely destroyed by self-digestion. Kidney and pancreas were normal, and the liver was of normal size and gray upon section.

Upon microscopic examination the thymus showed hyperplasia of the lymphoid elements. Hassal's corpuscles, which were numerous, showed a degeneration. There was a general hyperplasia of the lymphoid elements of the intestine.

The Albumin Content of Whey.—C. B. GRULEE (*Archives of Pediatrics*, June, 1904) gives the results of his experiments in determining the albumin content of whey.

The proteid percentage of whey, as given by various writers, ranges from 0.86 per cent. (König) to 1.02 per cent. (White and Ladd).

The writer obtained the following results: The average of a number of examinations was 0.5013 per cent., the highest 0.6616, and the lowest 0.2928 per cent. The work was conducted in the Laboratory of Physiological Chemistry of Northwestern University Medical School, and the following method was used: skimmed milk of pure quality and known to be stable in regard to the percentage of its constituents, was taken and raised to a temperature of 106° F., and rennet added in the proportion of one grain to the quart. After thirty minutes the curd was broken and removed by filtering through a wire sieve. The whey was heated to 150° F. to destroy the enzyme.

The whey was again filtered through Swedish filter paper, the sediment being small in amount. To 25 c.c. of this filtrate was added 1 c.c. of 25 per cent. acetic acid and three or four drops of 10 per cent. ammonium hydroxide and distilled water to make 100 c.c. This was boiled thoroughly and set aside until the coagulated albumin had settled.

The clear fluid was decanted through a Gooch crucible and distilled water added to the albumin left in the beaker. The supernatant fluid was treated in this manner several times, and the albumin was finally washed three times and then dried at 105° C. for two hours, at the end of which time it was cooled and weighed.

The drying and weighing were repeated until no difference in weight was obtained.

The writer believes that the various results obtained by experimenters in this line have been due to: 1. The milk. 2. The method of preparation of the whey. 3. The method of determination of the amount of albumin.

It is probable that most experimenters have prepared the whey by the use of liquid rennet and have determined the amount of albumin by the Kjeldahl process.

The writer used powdered rennet and the gravimetric process as described.

This method evidently procures a more perfect curding of the casein and leaves for the infant the more easily digested proteids.

Pollakiuria and Enuresis of Hysterical Origin in Children.—O. REINACH (*Jahrbuch für Kinderheilkunde*, 1903, Bd. viii., S. 795) reports two observations in children. The first patient was a girl, aged two years, intelligent and well developed, whose mother showed all the stigmata of hysteria, and whose father was neurasthenic. Following a terrifying dream, the child developed pollakiuria, voiding urine twenty

to thirty times in the twenty-four hours, and as frequently by day as by night. Sometimes she wet the bed, though she usually waked and cried vociferously. After this condition lasted two months the author conceived the idea of submitting her to painful faradization. This means of suggestion succeeded at once and prompt cure resulted. The same procedure was successful in the second patient, a girl, aged ten years, whose mother was manifestly hysterical.

GYNECOLOGY.

UNDER THE CHARGE OF

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Castration after Hysterectomy.—BLUHM (*Zentralblatt für Gynäkologie*, 1904, No. 28) reports the case of a virgin, aged forty years, whose uterus was removed for malignant disease, the ovaries and tubes being spared. After the lapse of nearly two years she began to have such severe menstrual molimina that it was necessary to extirpate the ovaries. The writer thinks that this phenomenon is more apt to follow hysterectomies for cancer than for fibroid, hence he strongly advises the removal of the adnexa in the former cases, aside from the risk of metastasis.

Alexander's Operation.—STEIDL (*Zentralblatt für Gynäkologie*, 1904, No. 28) reports 60 cases extending over a period of two and one-half years; 38 for simple retrodisplacement, and 22 for retroflexion with prolapsus. He makes a crescentic incision above the pubes and does not open the canal. Non-absorbable sutures are used, and the wound is always drained. The patient is allowed to leave the hospital at the end of two weeks(!). Suppuration occurred in 12 cases. Of 49 patients who were examined at intervals of from two months to two and one-half years after operation all but 2 were permanently cured.

Primary Carcinoma of the Clitoris.—JACOBY (*Zentralblatt für Gynäkologie*, 1904, No. 30) reports two cases in which he operated, both having a recurrence in the inguinal glands. He collected reports of sixty-five other cases. The writer advises that every case of obstinate pruritus or eczema of this region should be regarded with suspicion as a possible forerunner of malignant disease, and in the event of enlargement of the organ a piece should be removed for microscopic examination. The only operation is extensive excision with thorough cauterization.

Results of Operation for Retroflexion and Prolapsus—BAATZ (*Zentralblatt für Gynäkologie*, 1904, No. 30) reports 217 operations for pro-

lapsus extending over a period of five years. His conclusions are as follows: All cases of prolapse of the vagina without retroversion should be treated by extensive plastic operations. In cases in which there is accompanying retroversion and prolapsus, with or without fixation of the uterus, ventrofixation should also be done. Vaginofixation with plastic operations is indicated in patients who have passed the climacteric, and rarely in cases of complete procidentia. In short, the writer prefers ventrofixation to shortening of the round ligaments as the routine treatment of retroflexion, whether the uterus is adherent or mobile.

Origin of Broad Ligament Cysts. — HANDLEY (*Journ. Obst. and Gyn. of British Empire*, 1903, No. 11) advances the ingenious theory that all cysts of the broad ligaments situated above the tubes, and which can be enucleated, develop through the distention of accessory tubes. This he infers because he has found such cysts communicating with normal Fallopian tubes, and showing on their inner walls folds identical with those found in specimens of hydrosalpinx.

Isolation of the Pelvic Cavity with a Flap of Peritoneum and Fascia. —KRÖNIG (*Zentralblatt für Gynäkologie*, 1904, No. 31) recommends this method of shutting off the pelvic from the general peritoneal cavity, especially after abdominal hysterectomy for cancer of the uterus. Instead of using peritoneal flaps alone, he strips off the parietal fascia also, both anteriorly and posteriorly. Two cases are reported, one of which terminated fatally.

Cause of Hemorrhage in Fibroids.—THEILHABER and HOLLINGER (*Archiv für Gynäkologie*, Band lxxi., Heft 2) from an examination of nineteen fibroid uteri demonstrated the erroneous nature of the view that the bleeding in these cases is due to hyperplasia of the endometrium. Atrophy of the mucosa was more often present than hypertrophy. The writers believe that the "myofibrosis" of the uterine wall is the true cause. In consequence of this condition the vessels cannot contract normally during menstruation. Muscular contractions in the tumor and excessive congestion from psychical influences are other factors.

Anatomy of Placental Polypi. — CURTIS and OUI contribute an extended article on this subject to the *Annales de Gynécologie et d'Obstétrique*, July, 1904, of which the following is a summary: The structure of placental polypus, or so-called *deciduoma benignum*, is more complex than is usually supposed. It includes both the fetal and the maternal elements of the placenta, has a special vascular supply, and is capable of continuous growth, like a true neoplasm. Its nutrition depends on variations in the maternal circulation, the imperfectly obliterated intervillous spaces being in direct communication with the vessels in the submucosa. The layer of Langhans and the syncytium tend to proliferate, but there is never any tendency to invasion of the uterine tissue, as Michaelis claims. The writers disagree with Hartmann and Toupet, who claim that the distinguishing feature of these polypi is the presence of bloodvessels in the chorionic villi. They regard the persistence of the syncytium as the principal element in the

diagnosis, since the latter cannot exist without a free vascular supply. The most important inference is that such polypi under unknown conditions may become malignant.

DERMATOLOGY.

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Papilloma of the Sole.—T. D. BERRY (*Journal of Cutaneous Diseases*, May, 1904) reports a personal case of this disease and refers to the case described by D. W. Montgomery in the *Journal of the American Medical Association*, July 11, 1903. The author, while designating the disease "papilloma," throughout his remarks refers to it as a wart. It was extremely rebellious to all manner of treatment, being finally cured by the Paquelin cautery, burning entirely through the skin of the sole and into the fatty cushion beneath, and then turning the point round and round until there was a hole left in which the blunt end of a lead-pencil could have been inserted. Six months later there was no recurrence.

Effect of Becquerel Rays upon Tissues.—HALKIN (*Arch. für Derm. und Syph.*, 1903, lxv. p. 201) found that the bloodvessels seem to be first affected, but that the action on these structures cannot be regarded as the cause of the other phenomena, much less that of the inflammation. There appears to be a lack of resistance of the bloodvessels due to a form of paralysis. In normal and in lupus tissues, after prolonged exposure daily for nineteen days, cellular degeneration, dilatation of the vessels, and hemorrhage was noted in the superficial layers, but the deeper layers were not affected.

A Series of Cases Treated by Radium.—HARTIGAN (*British Journal of Dermatology*, March, 1904, p. 105) brought before the Dermatological Society of Great Britain and Ireland a number of cases of cutaneous disease, chiefly rodent ulcer and lupus. The radium used weighed ten milligrams, and was contained in an excavation at the end of a vulcanite screw and covered with a mica plate, which in turn was secured by a brass cap having a window in it. It fitted into an outer vulcanite case, admitting of the screw being withdrawn or projected. The results obtained were very encouraging.

Reference may be made in particular to a case of nævus vasculosus or "port-wine mark" in a woman, aged twenty-six years, which had existed from birth, having since then extended somewhat. It was on the left cheek, extending from the eyelid to the upper lip and on the nose. The upper half received in all eight applications and the lower three

applications, each of ten minutes' duration, and invariably after two or three applications a smart reaction followed, with vesication and the subsequent formation of scars, which later appeared as distinct, white areas.

Treatment of Lupus and Cancer by Light and Roentgen Rays.—R. B. WILD (*Medical Chronicle*, December, 1903) found that the Lortet-Genoud lamp was not so effective as the Finsen lamp or the Roentgen rays. For ulcerated surfaces and large areas the Roentgen rays were more useful than the lamp. Excessive reaction is cautioned against, the best results having been obtained when the reaction did not occur or was slight. In carcinoma the results were not satisfactory. Out of ten inoperable cases there was a fatal termination in nine, although in these cases pain was relieved and the discharge lessened.

Granuloma Fungoides Successfully Treated with X-rays.—LUSTGARTEN (*Journal of Cutaneous Diseases*, April, 1904, p. 185) records a case in which treatment succeeded after a long treatment of arsenic hypodermically administered had failed. The itching was a very notable and distressing symptom, which practically ceased after the first exposure. The lesions were fungoid and were widely distributed. A mild degree of inflammation of the skin developed under repeated exposures, but disappeared within a week, with a shedding of the epidermis. The patient was singularly susceptible to the rays, for a single twenty-minute exposure would produce an inflammation of the skin on any part of the general surface, followed by a complete disappearance of the lesion.

ELLIOTT (*ibid.*) has also observed excellent results from the same treatment in this disease, a case being referred to in which seventy-two exposures caused complete disappearance of all the lesions. Not all cases, however, are improved by this method of treatment, according to the experience of Dr. Duhring in a certain case.

The Staphylococci of Chronic Eczema.—F. VEIEL (*Münchener med. Wochenschrift*, January 6, 1904) examined cases of eczema madidans, moist and crusted, and found that in all forms and in all stages these organisms were present—generally yellow, sometimes white, and occasionally lemon colored. With few exceptions they existed in pure cultures. Tests were made to distinguish the saprophytic from the pyogenic forms, with the result that in every case the staphylococci of eczema seemed to be the same as the pyogenic forms, and the question is put forth, What part do they play in the production of eczema? It does not appear that anyone has been able by inoculation to have produced a chronic eczema, but it is highly probable that they must be regarded as influencing the disease and its course.

Creeping Eruptions.—L. P. HAMBURGER (*Journal of Cutaneous Diseases*, May, 1904) considers the whole subject at length. It has a special dermatological importance, and is worthy of note from a general medical standpoint because of its relation to myiasis, especially as applies to the bot-fly. The buttock is often the seat of the disease, pointing to the toilet as the possible seat of contagion. The feces may also be the carrier of the larvæ. The author describes a case occurring

in an imbecile boy, the lesion in the skin consisting of a serpiginous, curling, purplish, brownish, slightly crusted line situated on the right buttock, which gradually spread until an area the size of a hand was included. Excision of a piece of skin failed to discover a suspected parasite, but following the excision the line faded and the process ceased. Reference is made to the literature. The disease occurs more frequently in Russia than elsewhere, due to the bot-fly larvæ, but the parasite often escapes detection in a search for it.

Hyperidrosis Treated by Roentgen Rays.—ENGMAN (*Interstate Medical Journal*, 1903, x., p. 377) treated a case of this disease affecting the axillæ for three months until a dry erythema was produced, with loss of hair, with the result that there was improvement amounting to 50 to 75 per cent. Stelwagon (*Journal of Cutaneous Diseases*, 1903, xxi.) also found the same agent useful in sweating of the palms.

A Case of Bullous Lichen Planus.—M. F. ENGMAN (*Journal of Cutaneous Diseases*, May, 1904) reports a case, and concludes that the bleb formation is not a part of the pathological process, but that it may form in certain cases upon additional injury to the tissues through friction or accidental violence. It is a rare occurrence. The designation lichen planus pemphigoides would seem an appropriate name for the manifestation. A good photograph accompanies the article.

Dermatitis Exfoliativa Neonatorum, or Ritter's Disease—A. G. PATEK (*Journal of Cutaneous Diseases*, June, 1904) gives a case of this disease (rare in this country, although Ritter, in Germany, in ten years observed nearly 300 cases), and states that it is liable to be confounded with pemphigus foliaceus, acute pemphigus, and syphilis. The clinical history points to a septic nature, which view is corroborated by Ritter's experience, that it occurred in epidemics in foundling asylums. It is infectious, though Ritter has much evidence to show that contagion plays no part in its spread.

Patek found diplococci in the serum of lesions, but states that a diplococcus has been found also in pemphigus, observers remarking upon its resemblance to the gonococcus. Most observers have, however, isolated a micrococcus that in two cases gave rise, upon inoculation, to typical pemphigoid bullæ. It is probable, the author thinks, that there is confusion in the diagnosis of the two diseases, although it is possible to make a correct diagnosis.

Dermatitis Herpetiformis in Children.—MEYNET and PEHU (*Annales de Derm. et de Syph.*, December, 1903) conclude that the disease occurs more often in the later than in the earlier period of childhood, from six to ten years being the commonest period; that males are more affected than females (17 to 7); that no single cause can be stated to exist in the majority of cases, and that there is no reason for making a distinct group of children's cases as proposed by Unna.

Acute Infectious Pemphigus in a Butcher.—J. T. BOWEN (*Journal of Cutaneous Diseases*, June, 1904) finds this case interesting, because it occurred at a period when epizoötic foot-and-mouth disease prevailed in New England, a year ago. The eruption of blebs was evi-

dently due to an infection from a wound in a man engaged in butchering. Reference is made to the reports of like cases by Pernet and others. The evidence is not sufficient to prove that the virus of foot-and-mouth disease (usually mild both in animals and man) was a factor in this case. In acute pemphigus no other agent than an inoculated infection seems tenable, the process being a febrile infectious disease running an acute course.

Histological Investigation of Some Well-known Reducing Drugs in Skin Diseases.—VIGNOLO LUTATI (*Monatshefte f. Prakt. Derm.*, March 15, 1904) experimented on a cock's comb with tar, anthrarobin, gallacetophenon, and ichthyol. The action of tar is not merely superficial, but extends deep into the corium. Oleum rusci is more stimulating than oleum cadinum. Anthrarobin acts similarly to chrysarobin, and the author thinks that it might well replace the latter in practice.

Gallacetophenone is less stimulating than pyrogallol, more so than anthrarobin, and more like chrysarobin. The changes observed under the microscope are given in full.

Treatment of Various Forms of Cutaneous Disease by X-rays and Light.—W. A. JAMIESON (*Scot. Med. and Surg. Journ.*, February, 1904) refers to 133 cases of lupus vulgaris treated by himself during eighteen months, a large proportion being treated by the *x*-ray, others by the London Hospital modification of the Lortet-Genoud lamp. The latter method is regarded as superior in lupus to the *x*-ray in that it did not produce burns, although less useful, owing to its restricted employment and slowness of action, and consequently he has abandoned it, inasmuch as the beneficial effect was not commensurate with the expense. The results in rodent ulcer with the *x*-rays were good, and he advises, first, the removal of the growth by scraping, followed by chromic acid fused on the point of a probe applied to restricted areas at a time. Excellent results were obtained in mycosis fungoides.

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

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Bacilli in the Air Exhaled by Consumptives.—It has been accepted very generally that the air exhaled by consumptives during quiet respiration contains no tubercle bacilli or other bacteria, but this has been shown by Dr. W. Koelzer (*Zeitschrift für Hygiene und Infectionskrankheiten*, xliv., p. 217) to be not wholly true. This general belief is based upon the fact that even fairly strong currents of air are incapable of taking up bacteria, moulds or other matters from moist surfaces, unless at the same time the latter are subjected to some mechanical violence. Koelzer experimented with fifteen patients, who were allowed to breathe gently for from seven to fifteen minutes against sterile Petri dishes held two to three inches away from their mouths, proper pre-

cautions being taken to exclude all possible error from coughing, sneezing, speaking, and forced respiration. Of thirty guinea-pigs inoculated with the gelatine contents of the dishes, but one became infected; and this one died in ten weeks of typical general tuberculosis. It is especially significant that the dish the contents of which this animal received was one which was exposed to the patient who was the sickest of the group and the only one with laryngeal lesions. The liberation of the bacilli in this instance is attributed to the constant vibration of the vocal cords or to the bursting of minute bubbles, which occurs when the moist cords move apart from each other. It is suggested, however, that bacilli may be given off to the respired air by the bursting of bubbles (rales) in the fine bronchi, for the bursting of every bubble of mucus is accompanied by liberation of the finest particles of fluid, invisible to the naked eye, some of which may not fall back and become attached again to the surface of the tube, but may escape to the outer air. Naegeli and Buchner demonstrated more than twenty years ago that the bursting of fine bubbles caused by the ascent of air currents through a bed of sand impregnated with pure cultures of bacteria, projected bacteria four inches vertically. Since particles of coal-dust may reach the alveoli in inspiration, there can be no doubt that equally minute particles from the lungs may escape during expiration. Foelzer expressly disclaims any suggestion that his results are of any great practical importance, for the number of bacilli expelled in this way must be as nothing to those in suspension from dried and pulverized sputum and from sprayed droplets caused by coughing, sneezing, and speaking. His conclusions are summarized as follows: 1. The sentence "The air of quiet respiration of consumptives is free from tubercle bacilli" should be amended to read as follows: "The air of quiet respiration of consumptives is not germ-free, yet the exhalation of tubercle bacilli occurs only under peculiar conditions, and then to such a slight extent that, from a practical point of view, the expired air may not be considered as an essential source of infection." 2. The source of the infectivity of respired air is the spraying of mucopurulent material in the lungs, which we hear as rales. 3. The bacilli liberated in quiet expiration are so few in number that they can easily escape exact experimental demonstration. 4. The possibility of infection through quiet respiration is very remote in comparison with that offered by the pulverization of sputum and the spraying of sputum in coughing, sneezing, and speaking. 5. Severe laryngeal tuberculosis favors the infection of expired air quantitatively to such an extent that the bacilli can be exhaled in numbers sufficient for experimental demonstration.

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